TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION

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Submitted By

DR. AARTI GUPTA

DEPARTMENT OF PSYCHIATRY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA, PUNJAB

DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled **"TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION"** submitted towards partial fulfillment of the requirements for the award of **MD** in **PSYCHIATRY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **DR. RANJIVE MAHAJAN**, Professor & Head, Department of Psychiatry and **DR. NAVKIRAN S. MAHAJAN,** Professor, Department of Psychiatry No part of this thesis has formed the basis for the award of any degree previously.

_____

DR. AARTI GUPTA
Department of Psychiatry
Dayanand Medical College & Hospital,
Ludhiana, Punjab

Date:

Place:

CERTIFICATE OF SUPERVISORS

This is to certify that the work incorporated in this thesis entitled "**TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION"** has been carried out by **Dr. AARTI GUPTA** under our direct supervision. The data incorporated in this thesis is original and genuine and has been carried out by the candidate herself.

Signature of Supervisor

Dr. Ranjive Mahajan
Professor & Head
Department of Psychiatry
DMC&H, Ludhiana

Signature of Co-Supervisors

Dr. Navkiran S. Mahajan
Professor
Department of Psychiatry
DMC&H, Ludhiana

Date:

ENDORSEMENT BY THE HEAD OF THE INSTITUTE

This is to certify that the thesis entitled **"TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION"** is a bonafide research work done by **DR. RANJIVE MAHAJAN**, Professor & Head, Department of Psychiatry and **DR. NAVKIRAN S. MAHAJAN,** Professor, Department of Psychiatry in this institution.

Principal

Dr. Sandeep Puri
Principal
DMC&H, Ludhiana

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Signature

Dr. Aarti Gupta
Department of Psychiatry,
Dayanand Medical College & Hospital,
Ludhiana, Punjab - 141001

Date:

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Dedicated

to

My Family,

Friends

&

Teachers

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"Live as if you were to die tomorrow. Learn as if you were to live forever"

-Mahatma Gandhi

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ABBREVATIONS

BD	Bipolar Disorder
DSST	Digit Symbol Substition Test
IDEAS	Indian Disability Evaluation and Assessment Scale
IQ	Intelligent Quotient
ISBD	International Society for Bipolar Disorders
PGI	Post-graduate Institute
SCWT	Stroop Colour Word Test
SD	Standard Deviation
TMT	Trail Making Test

ABSTRACT

INTRODUCTION: Recent studies have focused on the nature of cognitive dysfunction in bipolar patients. The purpose of the current study was to investigate cognitive performance of individuals with bipolar disorder compared to healthy control subjects during a well-established euthymic period.
AIM: To study the cognitive functions in patients of bipolar disorder in remission.

MATERIALS AND METHODS: The study was conducted on 100 patients in age group 18-65 years diagnosed as Bipolar Disorder in remission presented to the Department of Psychiatry, DMC&H Ludhiana and 50 healthy controls in age group 18-65 years. Age matched healthy controls were also recruited. To be eligible, patients had to meet the inclusion criteria and provide written informed consent before enrolment. The euthymic state was ensured on clinical interview of the patient. Their cognitive functions were assessed using neuropsychological assessment tests. The Functional assessment were assessed using Indian Disability Evaluation and Assessment Scale (IDEAS). The course of the illness was assessed using National Institute of Mental Health- Life Chart Methodology Clinician Retrospective Chart (NIHM-LCM).

RESULTS: Remitted bipolar patients performed significantly worse than controls in several measures of attention, memory and executive function after controlling for age, education and occupation. Predominant polarity was found to be manic. The disability scores depicted mild to moderate disability and was positively associated with total number of episodes and longer duration of illness. Lithium carbonate treated patients performed significantly worse than others mood stabilisers on cognitive tests.

CONCLUSION: The present study showed persistent cognitive impairment on inhibitory control, attention, processing speed and memory in a group of bipolar euthymic patients. Cognitive assessment should be incorporated in the routine examination of these patients. Prompt diagnosis and active treatment with medications and novel cognitive rehabilitation strategies could potentially reduce the cognitive morbidity associated with this disorder.

KEYWORDS: Cognition, Bipolar, Disability, India

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INTRODUCTION

Bipolar disorder is characterized by repeated (i.e., at least two episodes in which the patient's mood and activity levels are significantly disturbed, this disturbance consisting on some occasions of an elevation in mood and increased energy and activity and on others of a lowering of mood and decreased energy and activity [1].

Bipolar disorder is a severe psychiatric disorder characterized by fluctuations in mood. People diagnosed with bipolar disorder experience mood episodes of mania, depression, or mixed, consisting of a combination of manic and depressive symptoms [2]. They can also experience periods of time where they are free of mood symptoms or euthymic. The lifetime prevalence of bipolar disorder is estimated between 1.0 to 1.6% in the adult population [3], and has been estimated as high as 5% [4].

Originally it was thought that while in a euthymic mood state, the patient was essentially unimpaired and experienced a return to normal functioning [5]. In fact, bipolar disorder has been reported as being the sixth leading cause of disability worldwide in terms of global health burden [6]. Some studies have shown that while mood state improves and patients achieve symptom recovery, functional recovery continues to be impaired and many patients don't return to premorbid levels of functioning [7, 8].

Cognitive deficits are impairments in cognitive ability that is closely linked to the functioning of specific brain areas, neural pathways, or cortical networks [9]. In addition to impairments in functional outcome, research evidence has shown neurocognitive deficits in bipolar disorder. Neurocognitive deficits are impairments in cognitive ability that are closely linked to the functioning of specific brain areas, neural 2 pathways, or cortical networks. There has been a large focus in determining the presence of these deficits in severe mental illness. Research in this area has found that neurocognitive deficits are characteristic of many psychiatric disorders, and that they are present in addition to the more typical symptoms of a disorder [10, 11].

Neurocognitive deficits have been substantially documented in patients with bipolar disorder, and exist in the areas of executive functioning, verbal and visual memory, attention, and visuospatial ability [10,12]. Some of these deficits seem to be impacted by the mood state the patient is experiencing, while others continue through periods where the patient is generally asymptomatic or euthymic [10,13]. Research in bipolar disorder has consistently shown impairments in occupational and psychosocial functioning and neurocognitive abilities. The literature examining the association between these two areas is minimal and complicated by methodological issues. Small sample sizes, limited neuropsychological test batteries and poor measurement of functional outcome weaken the conclusions in these few studies. Some of the main findings of this research have shown a relationship between neuropsychological domains and functioning, specifically that executive functioning, verbal memory, and sustained attention, among other neuropsychological domains, are associated with psychosocial and occupational functioning [14-16].

The current study seeks to examine this relationship while also avoiding some of the limits of previous studies. First there are many challenges in the measurement of functional outcome, which make an accurate assessment of functioning difficult to obtain. There are a number of ways to measure functional outcome which include patient self-report, collateral reports, clinician ratings, direct observation of a behaviour in the actual setting it occurs, and performance-based measures in clinical settings [17]. All of these measures have certain limitations. Patient self-report measures may be unreliable and in psychiatric patients may be influenced by their psychopathology, while collateral reports may also be unreliable and may be difficult to employ, as some patients do not have a person that can report on them.

Clinician ratings are not as extensive as may be needed and do not contain domains useful to assess real-world functioning. Direct observation of behaviour over time in real-world settings is an extensive and costly procedure and while performance-based

assessments occurring in a clinical environment are similar to direct observation and easier to accomplish, they may be 4 contrived and have questionable validity [17]. The existing studies of the association between neurocognitive deficits and functional outcome in bipolar disorder rely on self-report or clinician ratings as the determination of outcome, which are hampered by the prior mentioned limitations.

Research on cognitive structure of bipolar disorders has increased during the last 10-15 years. These studies have shown that cognitive impairments include impairments in selective attention and attention maintenance, recall and recognition memory, verbal learning, verbal fluency, reaction time, psychomotor, and executive functions [18-20]. In addition, it has been reported that these impairments can be found at all periods of the disorder [21,22], including remission[23]. It has also been claimed that cognitive deficiencies were present in patients in the premorbid period [12,24,25] and in non-affected first degree relatives of the patients [26,27]. It was suggested that these impairments may develop due to five different etiologies including iatrogenicity, duration of active disease, neurodevelopmental or neurodegenerative processes, and genetic predisposition [28].

Cognitive dysfunction may affect everyday activities and the ability to work [29].Therefore, neurocognition has an important role in functional outcomes of patients with bipolar Affective disorder [30]. Most of the studies have focused on cognitive impairments in subjects during an episode, and very few studies have examined neurocognitive impairments in euthymic patients. Very few studies are available to comment on neurocognitive functions in Indian patients with Bipolar Affective Disorder (BPAD) during the euthymic phase.

Recently, there have been neuropsychological studies in which formal rating of symptoms were performed on younger bipolar patients in remission. Van Gorp et al. [31,32] described impairment of verbal memory and executive function, although executive function was only affected in those with a past history of alcohol dependence. Ferrier et al.[33] showed that patients were impaired on a range of

neuropsychological tests but that after co-varying for affective symptoms only specific executive function, especially working memory tests were significantly impaired in remission.

Current symptoms, past course of illness, clinical features such as the presence of psychosis and co-morbid conditions may all influence cognitive function in mood disorders With regard to psychiatric disorders, cognitive functions has been scarcely studied, but it is present implicitly in a large number of studies assessing premorbid intelligence as a key role in the development and outcome of psychiatric disorders. Cognitive functioning may contribute to functional outcome in Bipolar Disorder and may be applied in research and clinical interventions to prevent cognitive and functional impairment. Despite the general lack of assessment of cognitive function in clinical practice, clinicians are increasingly targeting cognitive symptoms as part of comprehensive treatment strategies. It is worth mentioning that neurocognitive impairment needs to be considered a therapeutic clinical target in order to improve both psychosocial functioning and quality of life of patients with BD (Grande et al., 2016) [34].

Findings of neurocognitive deficits that predict functional outcome could provide guidance to the clinical field and support the addition of neuropsychological measures to assess future outcomes of patients with bipolar disorder, which could also increase awareness in the field that mood symptoms are not the only factor impacting functional recovery. Assessing for these neurocognitive deficits could guide the treatment and future life goals direction of each patient. Treatments could also begin to include cognitive remediation, as has been seen in schizophrenia, to improve the cognitive functioning of select patients diagnosed with bipolar disorder, in order to increase likelihood of functional recovery.

The main aim of this study was to examine the neuropsychological profile in well-remitted bipolar out-patients with no history of alcohol or drug dependence. In particular, we aimed to resolve some of the discrepancies in the literature about whether remitted patients have

deficits in executive function, memory or both. Hence the study was done to determine the factors affecting cognitive functioning in individuals with bipolar disorder in the euthymic phase and to find out the association between illness-related factors and cognitive functions. This proposal seeks to build on prior research to assess cognitive functioning in Bipolar disorder. It would contribute to better understanding of cognitive symptoms as a part of comprehensive treatment strategies.

AIMS AND OBJECTIVES:

To study cognitive functions in patients of bipolar disorder in remission.

REVIEW OF LITERATURE

Significant evidence exists demonstrating cognitive deficits and brain structural and functional abnormalities in bipolar disorder. There were also literature to suggest that people with bipolar disorder suffer poor outcomes, however, one difficulty in interpreting the results of functional outcome studies stems from the fact that outcomes are measured in a variety of ways. When examining bipolar disorder, outcomes can be assessed through symptomatic recovery and clinical variables such as number of episodes, number of hospitalizations, and length of episodes. Outcomes had also been measured by observing psychosocial and functional capacity.

In terms of measurement of these outcomes, some studies had used more general measures such as a Global Assessment of Functioning (GAF) rating, whereas others had examined functioning more specifically as it relates to interpersonal, occupational and self-care abilities. Still in other studies, a functional recovery was a return to baseline functioning prior to hospitalization or first mood episode. An additional constraint in the research related to psychosocial/functional outcome in 28 bipolar disorder was the variability of functional domains assessed.

Van Gorp, W. G et al (1998) conducted a study in which twenty-five euthymic bipolar patients (12 with and 13 without a history of alcohol dependence) were compared with 22 normal control subjects on a neuropsychological test battery assessing a range of cognitive domains. The relationship between subjects' neurocognitive performance and the course-of-illness variables (lifetime episodes and duration of mania, depression, or both), as well as current lithium level, was determined. The results indicated differences across the groups, with the bipolar patients performing worse than controls on tests of verbal memory. Furthermore, bipolar subjects with a history of alcohol dependence had additional decline in executive (i.e., frontal lobe) functions when compared with controls. For subjects in the bipolar group, lifetime months of mania and depression were negatively

correlated with performance in verbal memory and several executive function measures. Their findings support the presence of persistent neurocognitive difficulties in patients with long-standing bipolar disorder who are not in the psychiatrically acute state or who are suffering the effects of alcohol abuse and suggest that there may be an aggregate negative effect of lifetime duration of bipolar illness on memory and frontal or executive systems [32].

A study was conducted by **Ferrier et al (1999)** to test the hypothesis that patients with euthymic bipolar disorder show neuropsychological impairment. A battery of neuropsychological tests (assessed attention, working memory, learning and executive function) was administered to three matched groups of subjects: good-outcome patients with bipolar disorder (n = 21); poor-outcome patients with bipolar disorder (n = 20); controls (n = 20). All patients were clinically euthymic, although some had sub-syndromal depressive symptoms. They found that patients performed worse than controls on a number of neuropsychological tests. When age, premorbid IQ and depressive symptoms were controlled for, the results indicated impairment of executive function. These findings provide evident support for the existence of neuropsychological impairment in patients with bipolar disorder in remission phase, although the possible effect of medication should not be overlooked. This may be of clinical relevance and raises questions about the course and outcome of the illness [33].

Rubinsztein J.S. et al (2000) conducted a case–control study of bipolar patients in remission. Bipolar patients were ascertained throughout-patients. They were included if they had been in remission for at least 4 months and if their psychiatrist obtained their permission to participate. Patients were diagnosed as having a bipolar I disorder using a case note review and structured interview. Subjects also had no history of substance dependence. The cognitive battery examined memory and executive function. Patients in clinical remission and having good social adaptation showed impairment on tests of visuospatial recognition memory. Accuracy on tests of executive

function was not impaired in patients in remission compared with controls, although response latency on these executive tests was still impaired. As our group and others had shown, patients with mania and unipolar depression show generalized impairment on tests of memory and executive function. In comparison, this study had demonstrated that patients in remission show a relatively specific impairment in memory with recovery of accuracy measures on executive function task. The increased response latency on the executive tasks suggests a possible small residual impairment. These findings suggest that in neuroanatomical terms, more posterior cortical function (temporal lobe) has not improved but there was at least some recovery of frontal lobe function in remission [35].

Akiskal HS et al (2000) conducted a systemic review to Re-evaluate the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. According to the authors, until recently it was believed that no more than 1% of the general population has bipolar disorder. Emerging data are beginning to provide converging evidence for a higher prevalence of up to at least 5%. Manic symptoms, even those with mood-incongruent features as well as mixed (dysphoric) mania are formally included in both ICD-10 and DSM-IV. Mixed states occur in an average of 40% of bipolar patients over a lifetime; current evidence supports a broader definition of mixed states consisting of full-blown mania with two or more concomitant depressive symptoms. Depression with antidepressant induced hypomania (sometimes referred to as bipolar III) also appear, on the basis of extensive international research neglected by both ICD-10 and DSM-IV, to belong to the clinical spectrum of bipolar disorders. Broadly defined, the bipolar spectrum in studies conducted during the last decade accounts for 30-55% of all major depressions. Rapid-cycling, defined as alternation of depressive and excited (at least four per year), more often arise from a bipolar II than a bipolar I baseline; such cycling does not in the main appear to be a distinct clinical subtype - but rather a transient complication in 20% in the long-term course of bipolar

disorder. Major depression superimposed on cyclothymic oscillations represent a more severe variant of bipolar II, often mistaken for borderline or other personality disorders. Atypical depressive features with reversed vegetative signs, anxiety states, as well as alcohol and substance abuse comorbidity, is common in bipolar patients. The proper recognition of the entire clinical spectrum of bipolarity behind such 'masks' has important implications for psychiatric research and practice. Conditions which require further investigation include: (1) major depressive episodes where hyperthymic traits - lifelong hypomanic features without discrete hypomanic episodes - dominate the intermorbid or premorbid phases; and (2) depressive mixed states consisting of few hypomanic symptoms (i.e., racing thoughts, sexual arousal) during full-blown major depressive episodes - included in Kraepelin's schema of mixed states, but excluded by DSM-IV. The concept of bipolar spectrum as used herein denotes overlapping clinical expressions, without necessarily implying underlying genetic homogeneity. In the course of the illness of the same patient, one often observes the varied manifestations described above - whether they be formal diagnostic categories or those which have remained outside the official nosology. Life charting of illness with colored graphic representation of episodes, stressors, and treatments received can be used to document the unique course characteristic of each patient, thereby greatly enhancing clinical evaluation [4].

A systematic review of the computerized literature of neuropsychological studies of BD published between 1980 and 2000 was conducted by **Quraishi S et al (2002).** Impairments when present were limited to acute episodes and to performance scores. Attention: attentional abnormalities were seen in symptomatic BD patients and persisted in remission in measures of sustained attention and inhibitory control. Memory: verbal memory was impaired even in euthymic patients while visuo-spatial memory deficits were variable depending on the tasks used. Executive function: all aspects of executive function (planning, abstract concept formation, set shifting) were impaired in

symptomatic BD patients. Performance on executive function tests was sensitive to the presence of residual symptoms but it may be normal in fully recovered patients. Comparison to other patient groups: no major differences in cognitive profile between BD and UP depression were found. Remitted BD patients out-performed stable schizophrenics on most cognitive measures but this advantage disappeared when they were acutely symptomatic. Symptomatic BD patients have widespread cognitive abnormalities. Trait related deficits appear to be present in verbal memory and sustained attention. Executive function and visual memory may be also affected at least in some recovered BD patients [36].

In a review article by **Savitz J et al (2005),** data from the imaging literature have led to suggestions that permanent structural brain changes may be associated with bipolar disorder. Individuals diagnosed with bipolar disorder display deficits on a range of neuropsychological tasks in both the acute and euthymic phases of illness, and correlations between experienced number of affective episodes and task performance are commonly reported. These findings have renewed interest in the neuropsychological profile of individuals with bipolar disorder, with deficits of attention, learning and memory, and executive function, asserted to be present. This paper critically reviews five different potential causes of neurocognitive dysfunction in bipolar disorder: (i) iatrogenic, (ii) acute functional changes associated with depression or mania, (iii) permanent structural lesions of a neurodegenerative origin, (iv) permanent structural lesions that are neurodevelopmental in origin, and (v) permanent functional changes that are most likely genetic in origin. Although the potential cognitive effects of residual symptomatology and long-term medication use cannot be entirely excluded, we conclude that functional changes associated with genetically driven population variation in critical neural networks underpin both the neurocognitive and affective symptoms of bipolar disorder. The philosophical implications of this conclusion for neuropsychology are briefly discussed [29].

A systemic review was conducted by **Robinson LJ et al (2006)** about evolution of cognitive impairment in bipolar disorder. A notion that sufferers of bipolar disorder achieve complete syndromal and functional recovery between illness episodes has been brought into question by evidence that a large proportion of patients fail to regain premorbid levels of functioning after the resolution of major affective symptoms. A growing body of evidence suggests that bipolar patients exhibit neuropsychological impairment that persists even during the euthymic state, which may be a contributory factor to poor psychosocial outcome. However, the aetiology of such impairment and its relation to progression of illness are not well understood. This review aims to consider evidence from studies investigating both the relationship between cognitive impairment and clinical outcome and studies of neurocognitive function in unaffected first-degree relatives (FDRs) of bipolar sufferers to address issues of the temporal evolution of cognitive impairment in bipolar disorder. In total, 150 full references were retrieved, from which 26 were determined to meet the inclusion criteria. Seven of the ten studies reported significant negative relationships between lifetime number of manic episodes and cognitive function. One study reported a relationship between manic episodes and impairment on a visual memory task. Six of ten studies reported significant negative relationships between lifetime number of depressive episodes and various measures of neuropsychological function. The weight of evidence suggests that greater neuropsychological dysfunction in bipolar disorder was associated with a worse prior course of illness, particularly the number of manic episodes, hospitalizations and length of illness. The most consistent finding was a negative relationship between the number of manic episodes and verbal declarative memory performance. Impairment in unaffected FDRs was reported in verbal declarative memory and some facets of executive function. Cognitive impairment may be a trait vulnerability factor for bipolar disorder that was present before illness onset and worsens as the illness progresses [12].

Ozdel O et al (2007) conducted a study in which twenty-seven euthymic patients (19 female, 8 male), diagnosed with bipolar disorder according to DSM-IV criteria were recruited from a patient sample routinely followed at the Mood Disorder Clinic of the Department of Psychiatry in Pamukkale University Hospital. All patients who met the inclusion criteria and gave consent enrolled to the study. The healthy controls were 21 subjects (16 female, 5 male) chosen among employees and relatives or acquaintances of the hospital staff working in clinical and administrative areas. Verbal and visual memory performance, attention, executive functions and psychosocial functions were evaluated for each participant. Bipolar patients showed significant attentional deficit and executive dysfunction and also poor performance on verbal and visual memory tasks compared to the controls. Illness duration and lifetime total episode number and previous episode with psychotic features was associated with worsened performance on attention, executive and memory tasks. Psychosocial functioning was not associated with cognitive deficit. The present study showed persistent cognitive impairment on inhibitory control and selective attention as well as poor performance on verbal and visual memory tests in a group of bipolar euthymic patients. The impaired neuropsychological performance was associated with duration of illness, total number of episodes per lifetime, and previous episodes with psychotic features. Attentional dysfunction seemed to be a trait abnormality for the sample studied [37].

Braw Y et al (2007) conducted a study in which they compared euthymic bipolar disorder patients with schizophrenic patients. Cognitive deficits are fundamental features in schizophrenia (SZ) and major determinants of psychosocial functioning. Cognitive deficits in bipolar disorder (BD) were only recently recognized, and research on them was limited, especially in the euthymic stage. Earlier attempts to establish and compare the cognitive profiles of these overlapping disorders were few, and their results were inconsistent. They compared the cognitive profile of age- and gender-matched euthymic BD patients,

SZ patients in remission, and healthy controls (30 subjects in each group). Braw Y et al (2007) conducted a study in which cognitive performance was evaluated using a well-validated computerized assessment battery (Cambridge Neuropsychological Test Automated Battery [CANTAB]). The findings indicated both quantitive and qualitative differences in cognitive functioning of patients who were in the stable stage of the two disorders. While SZ patients exhibited more generalized cognitive deficits, those of the BD patients were more focused in the domains of sustained attention and the executive functions (specifically, planning and set-shifting). The SZ patients were more impaired in cognitive functions associated with frontal lobe activity, tentatively implicating dorsolateral prefrontal functioning. The overall findings help clarify the cognitive profiles of the two disorders while emphasizing the need to conceptualize executive functions in terms of a number of different higher order cognitive processes. The findings also point toward cognitive domains that necessitate future research, which may eventually aid in differential diagnosis and cognitive rehabilitation of BD and SZ patients [38].

Trivedi J.K. et al (2008) conducted a study to assess neurocognitive functions in first-degree healthy relatives of patients with bipolar disorder and to compare them with healthy controls with no family history of any neuropsychiatric disorder, on parameters of executive functioning, working memory and vigilance, which are still under-researched neurocognitive domains in this context. Ten first-degree apparently healthy relatives of patients with bipolar disorder were compared with 10 age- and education-matched control subjects on computer-based cognitive tests. They found that as compared to the control group, the relatives group performed significantly poorly on tests for executive function and vigilance, while on the test for working memory the performance was not significantly different on most of the parameters. In conclusion, executive functioning and vigilance could be potential markers of the endophenotype in bipolar patients.[28]

Sanchez-Moreno J et al (2009) conducted an extensive Medline and Pubmed search of the published literature from 1980 up to December 2007, using a variety of search terms to find relevant articles. Bibliographies of retrieved papers were further analysed for publications of interest. Articles that reported clinically significant findings on functioning and disability, and research reports were reviewed in detail. From these articles, they determined that bipolar disorder was associated with significant impairment in work, family and social life, beyond the acute phases of the illness. The aspects that appear to increase the risk of low functioning and disability in bipolar patients are mainly subsyndromal symptoms and neurocognitive impairment, among others. Suitable pharmacological and psychological interventions may improve the level of functioning and reduce the disability in bipolar patients. Potential targets to be considered for intervention should be residual symptoms, comorbid conditions and neurocognitive deficits. Further research was required to better identify the factors that best predict functioning in bipolar patients [39].

Leboyer M et al (2010) conducted a systematic PubMed search of all English-language articles, published between 2000 and 2010, focusing on the English and French literature with bipolar disorder cross-referenced with the following search terms: emotional dysregulation, sleep and circadian rhythm disturbances, cognitive impairment, age at onset, comorbid medical and psychiatric conditions, psychosocial and medical interventions, outcome, remission, and personalized medicine. The search was conducted between July 2009 and July 2010. The literature on bipolar disorder was reviewed to provide supporting evidence that the assessment of various symptom domains that are dysfunctional between episodes should all be considered as core dimensions of the disorder. Forty-one articles were identified through the PubMed search described above and selected on the basis of addressing any combination of the search terms in conjunction with bipolar disorder. Current guidelines advocate the use of more or less similar treatment algorithms for all patients, ignoring the clinical,

pathophysiological, and lifetime heterogeneity of bipolar disorder. Systematic assessment of inter episodic dimensions, along with comorbid medical and psychiatric risk factors, should be performed along the life cycle in order to plan specific and personalized pharmacologic, medical, and psychosocial interventions tailored to the needs of each patient and ready-to-test biosignatures to serve as risk factors or diagnostic or prognostic tools. Medical and research findings, along with health economic data, support a more modern view of bipolar disorder as a chronic, progressive, multisystem disorder. This new comprehensive framework should guide the search to identify biomarkers and etiologic factors and should help design a new policy for health care, including prevention, diagnosis, treatment, and training [40].

Latalova K et al (2011) conducted a systemic review in which Medline and Psyc Info data bases were searched for articles indexed by the combinations of MESH term or key word “bipolar disorder” with the following terms: “cognition”, “memory”, “neuropsychology”, “neuropsychological tests”, “lithium”, “anticonvulsants”, “antipsychotics”, and “schizophrenia”. Constraints limiting time period of publications or their language were not applied. Reference lists of publications identified by these procedures were hand-searched for additional relevant citations. There is evidence of stable and lasting cognitive impairment in all phases of bipolar disorder, including the remission phase, particularly in the following domains: sustained attention, memory and executive functions. But research on the cognitive functions has yielded inconsistent results over recent years. There was a growing need for clarification regarding the magnitude, clinical relevance and confounding variables of cognitive impairment in bipolar patients. The impact of bipolar illness on cognition can be influenced by age of onset, pharmacological treatments, individual response, familial risk factors, and clinical features. In addition to the mood state, cognitive performance in bipolar patients was influenced by seasonality. Conclusion. Previous optimistic assumptions about the

prognosis of bipolar disorder were based on the success of the control of mood symptoms by pharmacotherapy. However, it was now clear that the “remitted” euthymic bipolar patients had distinct impairments of executive function, verbal memory, psychomotor speed, and sustained attention. Mood stabilizers and atypical antipsychotics may reduce cognitive deficits in certain domains and may had a positive effect on quality of life and social functioning [41].

According to **Sole B et al (2011),** bipolar disorder is a severe mental illness that affects nearly 4.4% of the general population when bipolar spectrum disorders are taken into account. Neurocognitive impairment is thought to be a core deficit of this illness since it is present during euthymia. In fact, 40-60% of euthymic patients present with neurocognitive disturbances. Not only the clinical factors but also disturbances in neurocognition can influence the functional outcome of BD patients. Hence, further research is needed in order to clarify the relationship between these variables. Despite the growing body of evidence that has emerged during the last decade, no unique neurocognitive profile has been proposed yet for either BD subtype. The majority of the studies recluted heterogeneous samples (including both bipolar I and II) or focused on BD-I patients only. The aim of this review is to give an overall picture of the main neurocognitive disturbances found in the bipolar spectrum and particularly in BD-II, where the findings are more ambiguous. An extensive review of all the literature has been done regarding this subtype (from 1980 until July 2009). Data available until now suggest that deficits are present across the bipolar spectrum (BD-I and BD-II), but they seem slightly more severe in BD-I. The extent to which either subtype share-or not-some similarities is still unknown. According to the authors, more studies are required but it would also be interesting to reach a consensus in the neuropsychological assessment of BD to facilitate comparisons between the different studies [42].

Doruk A et al (2014) conducted a study to investigate cognitive functions in the manic, depressed and remission periods of bipolar

disorder by comparing with a healthy control group. In recent research, it has been suggested that cognitive functions seem to be impaired not only during the acute phases of bipolar disorder, but also during remission. Cognitive functions including attention and memory were examined in 20 manic, 10 depressed and 21 euthymic bipolar I patients (3 months of remission, Hamilton depression scale score≤8, and Young Mania Rating Scale score≤6) as compared with 22 healthy subjects. All subjects were male, and their ages were between 20-45 years. Cognitive evaluation was carried out by the Serial Digit Learning Test, Auditory Verbal Learning Test, Cancellation Test and Stroop Test. They found that attention, memory and learning functions were worse in the manic and depressive patients than healthy controls or patients in remission and that the number of depressive episodes had a negative effect on attention functions. No difference was found between patients in remission and healthy controls. Some attention subtests scores were negatively related to the memory test and its subtest scores in manic and depressed patients. This study has shown that impairments in attention, memory, information processing and learning functions of bipolar patients were specific to the depressive and manic periods of the disorder and no effect was present in the remission period. Also, it was noteworthy that the impairment in memory functions in the manic episode was not only due to an effect of attention functions [43].

Daglas R et al (2015) conducted a systematic review of the evidence in the acute and remission phases of the illness. There is evidence of cognitive impairment that persists in the remission phase of bipolar disorder; however, the extent of the deficits that occur from the first onset of the disorder remains unclear. This was the first systematic review on cognitive functioning in the early stages of bipolar I disorder. The aim of the study was to identify the patterns and degree of cognitive impairment that exists from first-episode mania. A comprehensive search of the literature on cognitive functioning in FEM was undertaken using three electronic databases, MEDLINE

(Thompson Reuters Web of Knowledge), PubMed (United States Library of Medicine) and PsycINFO (Wolters Kluwer Health OvidSP). Across all three databases, the search generated 217 journal articles that made reference to the search terms in their titles and abstracts. Of the 217 articles identified, 134 remained after duplicates were removed. Full texts of the remaining articles were retrieved and assessed to determine whether they met the inclusion and exclusion criteria for this review. Eligible studies were separated into two groups: acute and remission. The Newcastle-Ottawa quality assessment scale was utilised to measure the quality of the included studies. A total of seven studies (three acute and four remission), including 230 first-episode mania and 345 healthy control participants, were eligible for the review. The studies in the acute phase only examined aspects of executive functioning, with impairments identified in cognitive flexibility, though not in response inhibition and verbal fluency relative to healthy controls. The most consistent finding during the remission phase was a deficit in working memory, whereas in the other domains, the findings were equivocal. Non-verbal memory and verbal fluency were not impacted in remission from first-episode mania. In conclusion, deficits are present in some but not all areas of cognitive functioning during the early stages of bipolar I disorder. Further research is warranted to understand the longitudinal trajectory of change from first-episode mania [44].

Bhatia P et al (2018) conducted a study which was an exploratory, single group, cross-sectional, and exploring the nature of neuropsychological functioning in euthymic phase of BPAD patients and further exploring the predictors of neuropsychological functioning in euthymic phase of BPAD. Patients in euthymic phase of BPAD for at least 3 months with minimum 2 years of illness duration in age group of 18–55 years of any gender, Hamilton Depression Rating Scale (HAM-D)<6 and Young Mania Rating Scale (YMRS)<7 and those who gave informed consent were inducted. A total of 60 bipolar disorder patients, currently in euthymic phase for the last 3 months with minimum

duration of illness 2 years, currently on medications were administrated various neuropsychological tests. Approximately half of the patients had neuropsychological impairments in the areas of mental speed, sustained attention, verbal fluency, working memory, set shifting, verbal and visual memory, and visual-constructional ability. The findings of the current study showed that the around half of euthymic bipolar disorder patients had some kind of neuropsychological impairments. Duration of illness, number of episodes, residual manic and depressive symptoms, and combination of medicines had a significant impact on neuropsychological functions. Hence, one should also focus on neuropsychological functioning while planning the pharmacological interventions for complete functional recovery in bipolar patients. The association of clinical factors with cognitive deficits showed in this study can help in predicting and segregating high-risk population for poor functional recovery and starts early initiation of cognitive remediation [45].

Miskowiak K. W et al (2018) conducted an ISBD Targeting Cognition Task Force paper which provided the first consensus-based recommendations for clinicians on whether and how to assess and address cognition in their patients. According to the authors, cognition is a new key treatment target in BD but there has been a lack of consensus on how cognitive impairment should be assessed and managed. The task force addressed questions about (I) whether and when to conduct cognitive screening assessments, (II) what screening tools are most feasible, (III) what the implications are if impairment is detected, and (IV) what treatment perspectives there are for improving cognition and functioning in BD. The task force, consisting of 19 international experts from nine countries, discussed the challenges and recommendations in a face-to-face meeting, telephone conference call and email exchanges. Consensus-based recommendations were achieved through these exchanges with no need for formal consensus methods. The identified questions were: (I) Should cognitive screening assessments be routinely conducted in clinical settings? (II) What are

the most feasible screening tools? (III) What are the implications if cognitive impairment is detected? (IV) What are the treatment perspectives? Key recommendations are that clinicians: (I) formally screen cognition in partially or fully remitted patients whenever possible, (II) use brief, easy-to-administer tools such as the Screen for Cognitive Impairment in Psychiatry and Cognitive Complaints in Bipolar Disorder Rating Assessment, and (III) evaluate the impact of medication and comorbidity, refer patients for comprehensive neuropsychological evaluation when clinically indicated, and encourage patients to build cognitive reserve. Regarding question (IV), there was limited evidence for current evidence-based treatments but intense research efforts are underway to identify new pharmacological and/or psychological cognition treatments. Key recommendations after this study are that clinicians: (I) conduct formal assessment of cognition for all patients in partial or full remission whenever possible, (II) use brief, feasible tools that include objective and subjective cognition measures such as the SCIP and COBRA, which exist in multiple languages and are freely available through the ISBD website, (III) evaluate the potential impact of medication, comorbidity and symptoms when impairment was detected, refer for more comprehensive neuropsychological evaluation when clinically indicated, and use the assessments to encourage patients to build up their cognitive reserve. Regarding (IV), there was currently no clinically available treatment with efficacy on cognition except for one recent positive CR trial. However, intense research effort was likely to reveal new effective pharmacological, psychological and multimodal treatments in the near future [46].

Pradip MA et al (2019) conducted a study in which fifty bipolar patients in the euthymic state confirmed through Young Mania Rating Scale ≤ 6 and Hamilton Depression Rating Scale ≤8 were compared with healthy comparison group on tests for assessing set shifting, verbal learning and memory, attention, short-term memory, and verbal fluency. The clinical variables – age of onset, number of episodes, and duration of

illness – were assessed to determine whether it influenced the neurocognitive functions. Euthymic bipolar patients performed worse than the comparison group in the areas of executive functions, verbal learning and memory, attention, short-term memory, and verbal fluency. The duration of illness and frequency of episodes significantly correlated with the neurocognitive deficits. The age of onset and mood stabilizers prescribed also influenced the cognitive functions in these patients. Cognitive impairments are found in bipolar affective disorder patients even in euthymic state. The duration of illness, number of episodes, age of onset, and medications affected the cognitive functions. This calls for prompt and effective management of the bipolar patients [47].

A study was done by **Ashenbrenner Y et al (2019)** to assess the level of cognitive impairment in patients with BD in remission. Many patients with bipolar disorder (BD) experience cognitive impairment (CI) in remission. The relationship of CI in patients with BD in remission with the presence of residual symptoms was not completely clear. The sample consisted of 64 adults with BD in remission (according to the DSM-V criteria), the average age – 36.77±5.81. The onset of the disorder – 27.44±4.06 years, the average duration of the disorder – 9.33±4.39 years. They provided a single examination of a patient including clinical interview and screening for CI with the Brief Neuropsychological Cognitive Examination (BNCE). They evaluated some of the cognitive measures using the TMT test. The first part A of the TMT test was used primarily to examine cognitive processing speed. The second part B of the test, in which the subject alternates between numbers and letters, was used to examine executive functioning. CI according to the BNCE was identified in 28 patients (43.75%) and corresponded to mild cognitive deficit. Patients with CI were characterized by low scores on the subtests «set of sequences» (patients with CI - 2±0.21; patients without CI – 2.67±0.44; $p<0.01$). The TMT test also showed the presence of statistically significant ($p<0.001$) attention deficits in patients with CI. CI manifested in a

decrease in processing speed, impaired switching and attention distribution. Residual symptoms were observed in 42.2% of patients in current remission. CI was linked with the presence of residual symptoms in remission (r=0.4; p=0.001). CI and residual symptoms occur in over 40% of patients with BD in remission. The detecting of both CI and residual symptoms in patients was statistically significant linked in their study. CI in BD should be considered as a potential therapeutic target. This data indicates the need to develop new approaches to BD treatment in remission [48].

Sachs G et al (2020) conducted a study to examine predictors of functional outcome in patients with bipolar disorder. Forty three remitted bipolar patients and 40 healthy controls were assessed with a neurocognitive battery testing specifically attention, memory, verbal fluency and executive functions. In a randomized controlled trial, remitted patients were assigned to two treatment conditions as add-on to state-of-the-art pharmacotherapy: cognitive psychoeducational group therapy over 14 weeks or treatment-as-usual. At 12 months after therapy, functional impairment and severity of symptoms were assessed. Compared to healthy controls, bipolar patients showed lower performance in executive function (perseverative errors $p < 0.01$, categories correct $p < 0.001$), sustained attention (total hits $p < 0.001$), verbal learning (delayed recall $p < 0.001$) and verbal fluency (p-words $p < 0.002$). Cognitive psychoeducational group therapy and attention predicted occupational functioning with a hit ratio of 87.5%. Verbal memory recall was found to be a predictor for symptom severity (hit ratio 86.8%). Recurrence in the follow-up period was predicted by premorbid IQ and by years of education (hit ratio 77.8%). Bipolar patients benefit from cognitive psychoeducational group therapy in the domain of occupational life. Deficits in sustained attention had an impact on occupational impairment. Implications for treatment strategies are discussed. Further evaluation in larger studies was needed [49].

Benjamin A et al (2021) conducted a study about factors affecting cognitive functioning in individuals with bipolar disorder in euthymic phase. Neurocognitive studies during the euthymic phase of bipolar disorder had shown persistent cognitive deficits in 32% of patients. There was limited evidence in the Indian literature regarding this area. Neurocognitive impairment can significantly affect the overall functional recovery of these individuals. Understanding potential factors contributing to neurocognitive impairment in bipolar disorder was essential to develop prevention strategies and effective treatments. A total of 50 patients with bipolar disorder currently in euthymic phase for the last three months with a minimum duration of illness of two years and current Young Mania Rating Scale <11and Hamilton Depression Rating Scale <8 currently on medications were administered various cognitive tests namely digit span test forward and backward, digit symbol substitution test and Trail making test A and B. The study was completed within a period of 6 months after getting approval from the institutional ethics committee. Patients with bipolar disorder, in remission, had cognitive impairment in attention, memory and executive functioning. More than 50% of the patients could perform digit span test forward more than five digits, and in the case of the digit span test backwards, more than 50% of patients could perform only less than or equal to three digits. In the Trail Making tests A and B,66% of the patients could perform within </=78seconds,and 62% could perform within </=273 seconds, respectively. Only 4% of the patients could complete 49 squares in the Digit symbol substitution test. Findings of the current study shows evidence of cognitive impairment in euthymic bipolar patients [50].

MATERIALS AND METHODS

Source of Data: This case control study was conducted on patients diagnosed as bipolar disorder presenting to Dayanand Medical College and Hospital, Ludhiana.

Sample Collection: The study included 100 patients in age group of 18-65 years with bipolar disorder in remission presented to the Department of Psychiatry in DMC & Hospital, Ludhiana and 50 controls in age group 18-65 years of age.

Inclusion Criteria:

For Cases:

1. The patients with a diagnosis of Bipolar Disorder in remission according to DSM-5 criteria presenting to DMC&H, Ludhiana.
2. Age group between 18 years to 65 years.
3. Duration of illness of at least one year.
4. Patients who gave consent for the study.

For Controls:

1. The patients not having any history of bipolar disorder or any other psychiatric illness.
2. Age group between 18 years to 65 years.
3. Individuals who gave consent for the study.

Exclusion Criteria:

For Cases:

1. Any other major psychiatric disorder in patients of Bipolar Disorder on AXIS I.
2. Suffering from an organic brain syndrome.
3. Patients who did not gave consent for the study.
4. Duration of illness less than one year.

For Controls:

1. Any on-going psychiatric or neurological disorder.
2. Current treatment with any psychotropic drugs.
3. Past history of bipolar disorder, schizophrenia, recurrent depression or other psychiatric disorder.
4. A first-degree relative with schizophrenia or bipolar disorder

Methodology:

The study was conducted on 100 patients in age group 18-65 years diagnosed as Bipolar Disorder in remission presented to the Department of Psychiatry, DMC&H Ludhiana and 50 healthy controls in age group 18-65 years. Age matched healthy controls were also recruited. To be eligible, patients had to meet the inclusion criteria and provide written informed consent before enrolment. The euthymic state was ensured on clinical interview of the patient. Their cognitive functions were assessed using neuropsychological assessment tests. The Functional assessment were assessed using Indian Disability Evaluation and Assessment Scale (IDEAS). The course of the illness was assessed using National Institute of Mental Health- Life Chart Methodology Clinician Retrospective Chart (NIHM-LCM).

Tools Used:

Sociodemographic Performa

1) **CLINICAL ASSESSMENT:**

A) National Institute of Mental Health- Life Chart Methodology Clinician Retrospective Chart (NIHM-LCM):

The clinician rated scale charts the phases of the illness for the entirety of a patient's life. Charting started with the first / index episode mentioning its polarity, and progresses alone each episode, this method allowed specification of the type of episode, its duration and severity. It also allowed the coding of comorbid symptoms, triggering life events, hospitalization, medication use and other relevant details. It charts the course of bipolar (or unipolar) recurrent affective illness, ongoing treatment, and important life events (Leverich & Post, 1996, 1997a, b, 1998). By constructing your own life chart you are creating a portable psychiatric history of your illness in the form of an easily understandable graph or picture that you and your physician can review together. The NIMH Life Chart Method (The LCM□) is easy to follow and provides a clear picture of the mood swings that are so typical of this illness. The life chart will provide you with a good

overview of the number of past episodes, their duration, frequency, and response to treatment.

B) **Indian Disability Evaluation and Assessment Scale (IDEAS)**:

The Indian Disability Evaluation and Assessment Scale (IDEAS) has been recommended for assessment and certification of disability by the Government of India (GOI).It is well suited for measuring disability in Indian population in which it has been validated. A scale for measuring and quantifying disability in mental disorders developed by the Rehabilitation Committee of Indian Psychiatric Society, December 2000. it. It evaluates disability in four areas (termed items in the scale), namely: I. Self-Care: Includes taking care of body hygiene, grooming, health including bathing, toileting, dressing, eating, taking care of one's health. II. Interpersonal Activities (Social Relationships): Includes initiating and maintaining interactions with others in contextual and socially appropriate manner. III. Communication and Understanding: Includes communication and conversation with others by producing and comprehending spoken/ written/non-verbal messages. IV. Work : Three areas are Employment/Housework/Education Measures on any aspect. 1. Performing in Work/Job 2. Performing in Housework 3. Performing in school/college. Each item is scored on a 5-point scale with a range of 0-4, i.e., from no (0) to profound disability (4). Add scores of the four items and obtain a total score which is further added to the duration of illness score to obtain global score. The alpha value at various centers was 0.8682, indicating good internal consistency between the items. It has good criterion validity and at face value, the instrument appeared to be measuring the desired qualities. Criterion validity was established by comparing IDEAS with SAPD (Schedule for the Assessment of Psychiatric Disability) which has been standardized in India.

2) NEUROPSYCHOLOGICAL ASSESSMENT

a) Attention:

Trial making test:

The trail making test (TMT) is a brief paper and pencil neuropsychological test often used for screening for cognitive impairment, principally attention and working memory. The TMT is a standard component of the Halstead-Reitan Battery which measures cognitive dysfunction. Both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper. In Part A, the circles are numbered 1 – 25, and the patient should draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1 – 13) and letters (A – L); as in Part A, the patient draws lines to connect the circles in an ascending pattern, but with the added task of alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.). The patient should be instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. Time the patient as he or she connects the "trail." Results for both TMT A and B are reported as the number of seconds required to complete the task; therefore, higher scores reveal greater impairment.

Digit span:

The Digit Span test was a subtest of both the Wechsler Adult Intelligence Scale (WAIS) and the Wechsler Memory Scales (WMS). Forward span captures attention efficiency and capacity. Backward span was an executive task particularly dependent on working memory. It has been comprised of two parts: Digit Span Forward and Digit Span Backward. Digit Span Forward requires the individual to repeat numbers in the same order as read aloud by the examiner, and Digit Span Backward requires the individual to repeat the numbers in the reverse order of that presented by the examiner. Test–retest reliability ranges from .41 to .83 for these tasks.

b) Processing Speed:

Digit symbol coding:

The DSST is a paper-and-pencil based cognitive test presented on a single sheet of paper that requires a subject to match symbols to numbers according to a key located on the top of the page. The subject copies the symbol into spaces below a row of numbers. The number of

correct symbols within the allowed time i.e. 90 seconds, constituted the score In this test the higher the score the better the person's performance. The DSST requires response speed, sustained attention, visual spatial skills and set shifting. It is part of the Wechsler Adult Intelligence Scale, one of the most widely used measures of intelligence.

c) Memory:

Postgraduate Institute (PGI) Memory Scale:

The Postgraduate Institute (PGI) memory scale is a part of the PGI battery of brain dysfunction, and has been developed in India. It has been constructed and standardised in 1977. It is a comprehensive scale to measure verbal and non-verbal memory and had been extensively used in Indian studies. It consisted of 10 sub-tests: remote memory, recent memory, mental balance, attention and con-centration (Digit span), immediate recall, verbal retention for similar pairs, verbal retention for dis-similar pairs, visual retention and recognition. Quintile norms were developed for the subjects in the age range of 20-45 years for the three educational level (i.e. 0-5,6-9 and 10+ above years of schooling) separately for each of the ten subtests. Reliability- for this, the test was re-administered on 40 subjects after an interval of one week. The test re-test reliability ranged between -70 and .84 for organic psychotic groups. .48 to .84 for neurotic normal group. Split half reliability was found to be .91 to .83 respectively. Validity: PGI Memory scale was found to have a correlation of .71 with Boton Memory scale and .85 with the Wechsler memory scale.

d) Executive function: Stroop Colour Word Test (SCWT):

The Stroop Color and Word Test (SCWT) is a neuropsychological test extensively used to assess the ability to inhibit cognitive interference that occurs when the processing of a specific stimulus feature impedes the simultaneous processing of a second stimulus attribute, well-known as the Stroop Effect. The Stroop Colour and Word Test (SCWT) measured the relative speeds of reading the names of colours (word

card), naming colours (colour card), and identifying colour names that were printed in another colour (interference card). As per the scoring method proposed by Golden (1978), the number of items correctly named in 45 s in each conditions is calculated (i.e., W, C, CW). Then the predicted CW score (Pcw) is calculated using the following formula: $Pcw = (W \times C)/(W + C)$. Then, the Pcw value is subtracted from the actual number of items correctly named in the incongruous condition (CW) (i.e., IG = CW − Pcw): this procedure allows to obtain an interference score (IG) based on the performance in both W and C conditions. Thus, a negative IG value represents a pathological ability to inhibit interference, where a lower score means greater difficulty in inhibiting interference. The test is essentially a measure of cognitive flexibility and response inhibition.

OBSERVATION & RESULTS

Table below indicates distribution of study subjects according to the demographic variables among cases and controls.

Table 1: Distribution according to the Age (in years)

Age	Cases (N=100)		Control(N=50)		Total	Chi-square value	p-value
	No.	%	No.	%			
< 30 years	28	28.0%	14	28.0%	42	2.136	0.711
31-40 years	23	23.0%	10	20.0%	33		
41-50 years	25	25.0%	11	22.0%	36		
51-60 years	15	15.0%	12	24.0%	27		
> 60 years	9	9.0%	1	2.0%	12		
Total	100	100.0%	50	100.0%	150		

Table 1 shows age wise distribution of the study subjects i.e patients of bipolar disorder and healthy controls. Majority of the patients of bipolar disorder 28% were in age group below 30 years followed by 25% in 41-50 years age group, followed by 23% in 31-40 years age group , 15% in 51-60 years age group and only 9 % in above 60 years age group. Majority of healthy controls 28% were in age group below 30 years followed by 24% in 51-60 years age group, 22% in 41-50 years age group, 20 % in 31-40 years age group and only 2 % in above 60 years age group.

It also shows association between groups and age. Chi-square test was used to explore the association between groups and Age. There was no significant difference between the two groups in terms of distribution of Age ($\chi 2 = 2.136$, $p = 0.711$).

Figure 1: Distribution in terms of Age

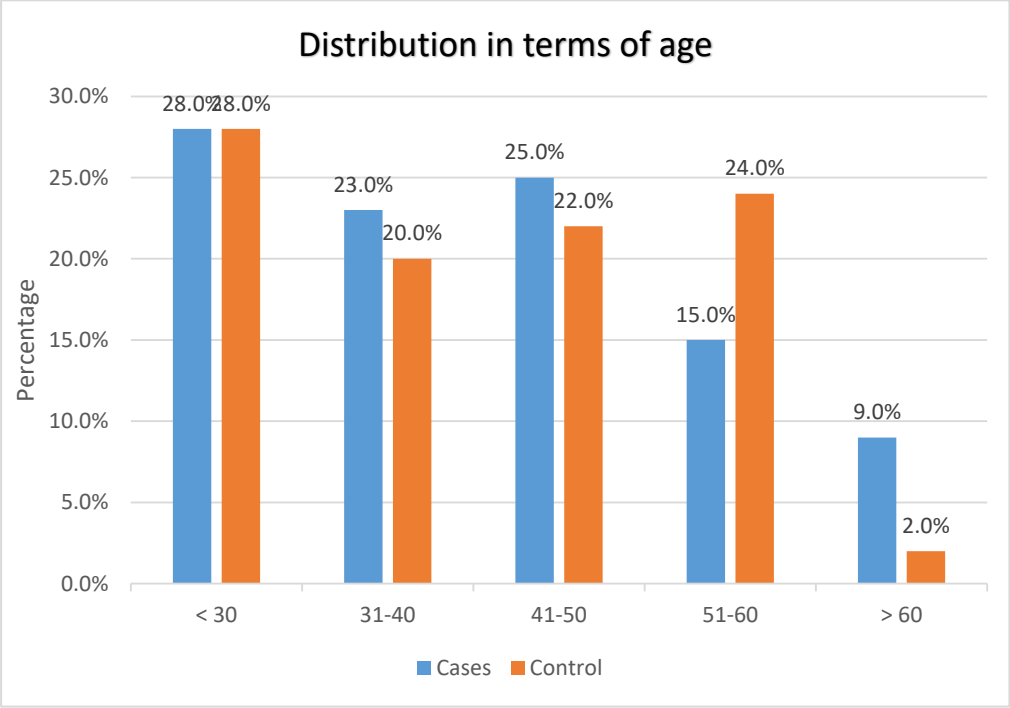

Figure 1 shows that majority of the patients i.e. cases 28% and controls 28% were in age group below 30 years.

Table 2: Distribution in Terms of Gender

		Cases (N=100)		Control(N=50)		Total	Chi-square value	p-value
		No.	%	No.	%			
SEX	FEMALE	20	20.0%	25	50.0%	45	14.286	0.001
	MALE	80	80.0%	25	50.0%	105		
TOTAL		100	100.0%	50	100.0%	150		

TABLE 2 shows gender wise distribution of the patients. 80 patients were male and 20 were females whereas in controls group, 25 were males and 25 were females. It also shows association between group and gender. Chi-squared test was used to explore the association between 'Group' and 'Gender'. There was significant difference between the two groups in terms of distribution of Gender ($\chi 2 = 14.286$, $p = 0.001$).

Figure 2: Distribution in Terms of Gender

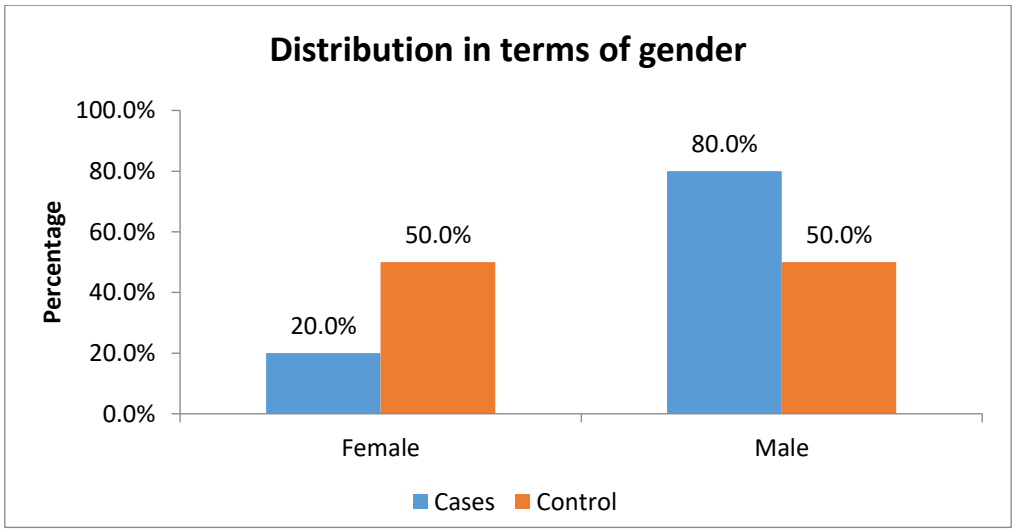

Figure 2 shows that majority of the cases were males i.e. 80% while controls had equal ratio of males and females.

Table 3: Distribution in Terms of Education

		Cases (N=100)		Control (N=50)		Total	Chi-square value	p-value
		No.	%	No.	%			
EDUCATION	ILLITERATE	6	6.0%	2	4.0%	8	3.378	0.848
	PRIMARY	1	1.0%	0	0.0%	1		
	MIDDLE	1	1.0%	0	0.0%	1		
	MATRICULATION	25	25.0%	14	28.0%	39		
	HIGHER SECONDARY	34	34.0%	17	34.0%	51		
	GRADUATE	27	27.0%	13	26.0%	40		
	POST-GRADUATE	6	6.0%	3	6.0%	9		
TOTAL		100	100%	50	100%	150		

TABLE 3 shows education wise distribution of the patients. 6 % Patients of bipolar disorder were illiterate. 1% of the patients had studied till Primary School, 1% of the patients had studied till Middle School, 25% of the patients had studied till Matriculation, 34% of the patients had studied till Higher Secondary and another 27% of the patients were Graduates and rest 6% of the patients were Post-Graduates or had an honors degree. In controls group, 4 % were illiterate, 28% of the patients had studied till Matriculation, 34% of the patients had studied till Higher Secondary and another 26% of the patients were Graduates and rest 6% of the patients were Post-Graduates or had an honors degree. It also shows association between group and education. Chi-square test was used to explore the association between Groups and Education. There was no significant difference between the two groups in terms of distribution of education ($\chi 2 = 3.378$, $p=0.848$).

Figure 3: Distribution of the Patients in Terms of Education

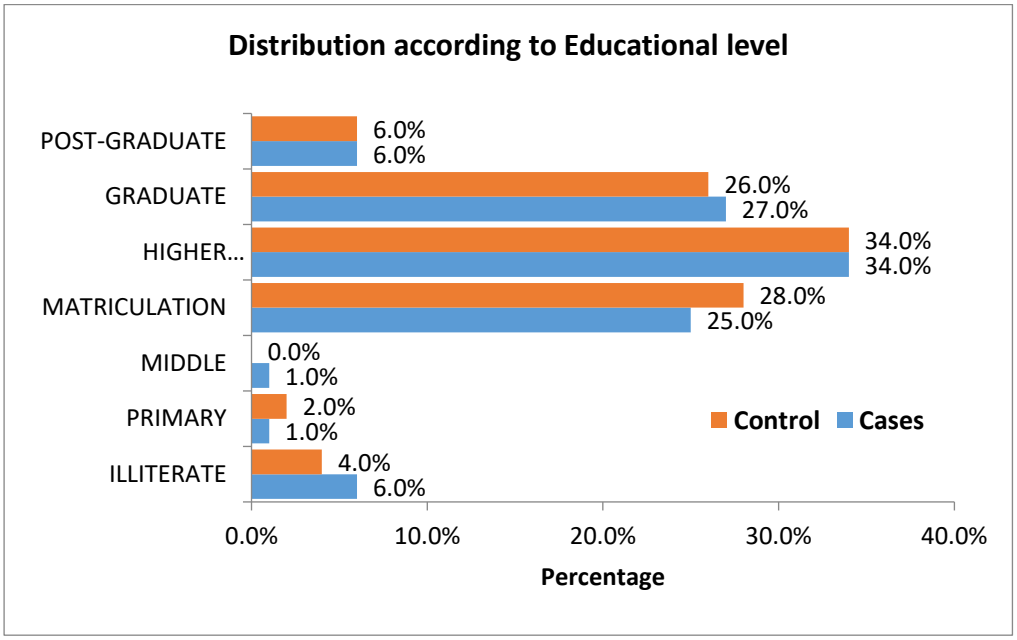

Figure 3 shows that majority of the patients of bipolar disorder (34%) and healthy controls (34%) were studied up higher secondary.

Table 4: Distribution of the Patients in Terms of Occupation

		Cases (N=100)		Control (N=50)		Total	Chi-square value	p-value
		No.	%	No	%			
OCCUPATION	UNEMPLOYED	32	32.0%	18	36.0%	17	11.36	0.078
	SEMI-SKILLED	0	0%	3	6.0%	3		
	SKILLED WORKER	44	44.0%	15	30.0%	37		
	SEMI-PROFESSIONAL	5	5.0%	5	10.0%	9		
	BUSINESSMAN	8	8.0%	1	2.0%	9		
	PROFESSIONAL	10	10.0%	8	16.0%	18		
	RETIRED	1	1.0%	0	0%	1		
Total		100	100%	50	100%	150		

TABLE 4 shows occupation wise distribution of the patients. Majority of patients (44%) were skilled workers, 32% were unemployed, 10% were professionals, 8% of the patients were businessman or self-employed, 5% were semi-professional, and 1% were retired. In controls group, majority i.e. 36% were unemployed, 30% were skilled worker, 16% were professionals, 10% were semi-professional, 6% were semi-skilled and 2% were businessman or self-employed.

It also shows association between group and occupation. Chi-square test was used to explore the association between Groups and Occupation. There was significant difference between the two groups in terms of distribution of Occupation ($\chi 2=11.36$, $p= 0.078$).

Figure 4: Distribution of the Patients in Terms of Occupation

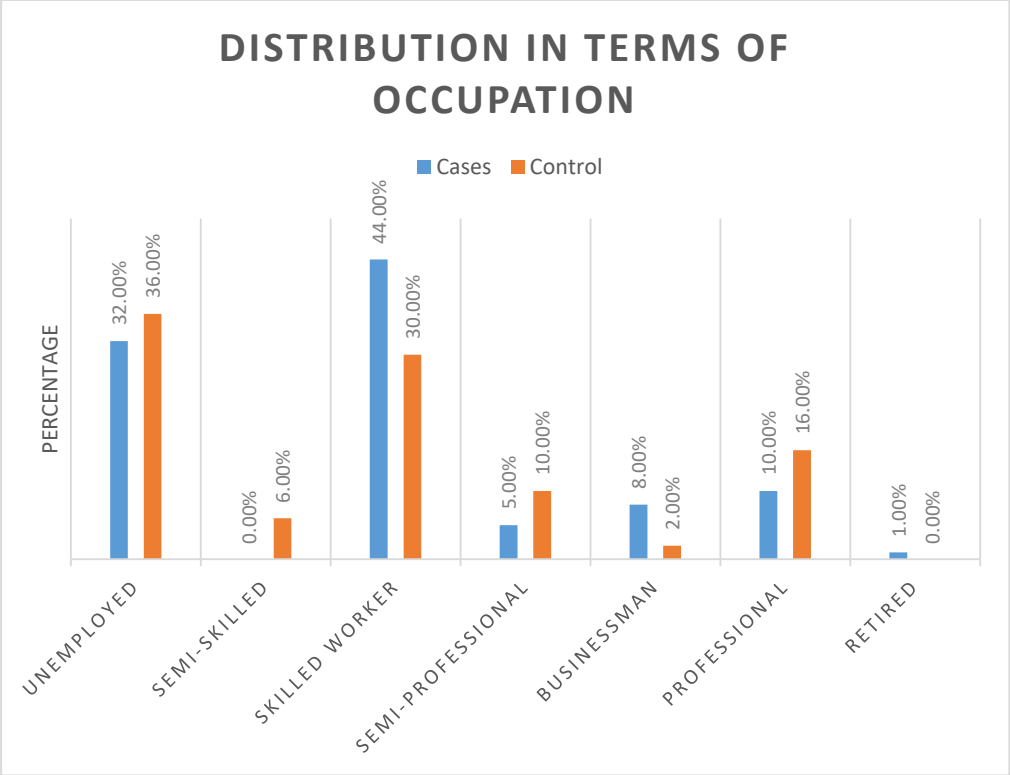

Figure 4 shows that majority of cases were skilled workers (44%) and majority of controls were unemployed (36%).

Table 5: Distribution of the Patients in Terms of Marital Status

		Cases (N=100)		Controls (N=50)		Total	Chi-square value	p-value
		No.	%	No.	%			
MARITAL STATUS	MARRIED	74	74.0%	41	82.0%	115	6.891	0.075
	UN-MARRIED	26	26.0%	9	18.0%	31		
TOTAL		100	100%	50	100%	150		

Table 5 shows distribution of the patients in terms of marital status. Maximum patients (74%) were married and rest 26% were unmarried. In controls group also, majority of the subjects i.e. 82% were married and rest 18% were unmarried. It also shows association between group and marital status. There was no significant difference between the two groups in terms of distribution of Marital Status ($\chi 2=6.891$, p=0.075).

Figure 5: Distribution of the Patients in Terms of Marital Status

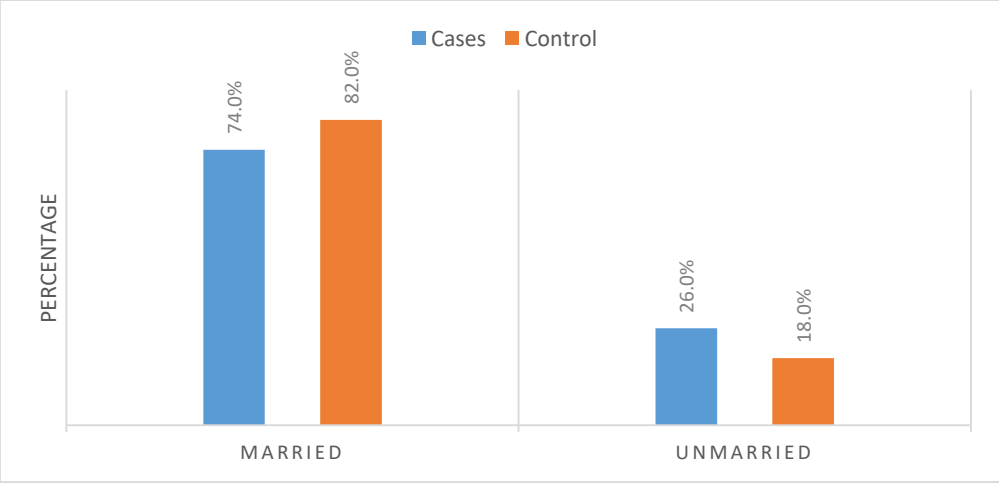

Figure 5 shows that majority of the patients (74%) and healthy controls (82%) were married.

Table 6: Distribution of the Patients in Terms of Family Type

		Cases(N=100)		Controls(N=50)		Total	Chi-square value	p-value
		NO.	%	NO.	%			
FAMILY TYPE	EXTENDED NUCLEAR	16	16.0%	10	20.0%	26	13.528	0.004
	JOINT	39	39.0%	6	12.0%	45		
	NUCLEAR	45	45.0%	34	68.0%	79		
TOTAL		100	100.0%	50	100.0%	150		

TABLE 6 shows distribution of the patients in terms of family type. Maximum patients (45%) were living in a nuclear family, followed by 39% of patients living in a joint family and only 16 % were living in a extended nuclear family. In controls group, majority i.e. 68% lived in a nuclear family followed by 20% in an extended nuclear family and only 12% in a joint family. It also shows association between group and family type. Chi-squared test was used to explore the association between Groups and Family Type. There was significant difference between the two groups in terms of distribution of Family Type ($\chi 2=13.528$, p=0.004)

Figure 6: Distribution of the Patients in Terms of Family Type

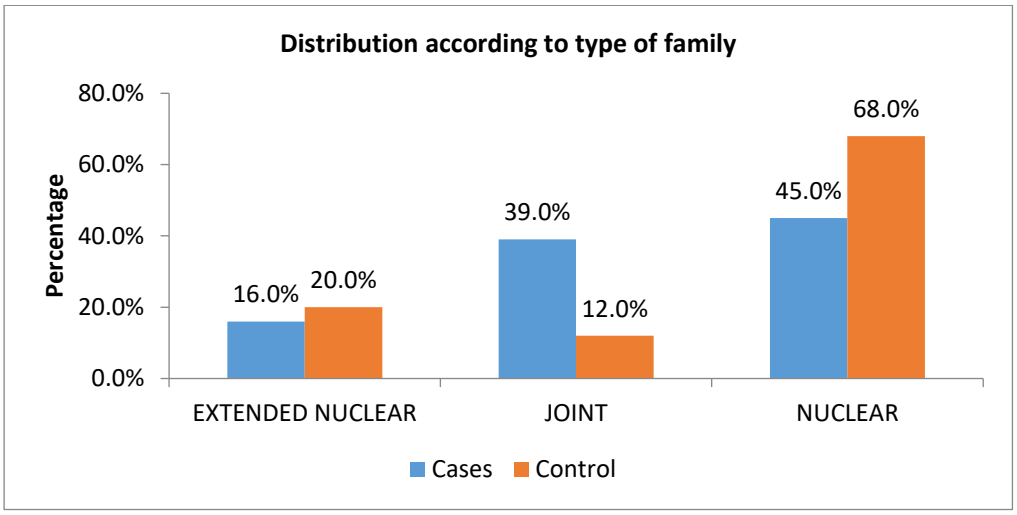

Figure 6 shows that majority of cases (45%) as well as controls (68%) had nuclear family.

Table 7: Distribution of cases in terms of family history (N=100)

FAMILY HISTORY OF BIPOLAR DISORDER		
	No. of cases	**Percentage**
None	90	90.00%
Present	10	10.00%

Table 7 below indicates distribution of study subjects according to qualitative variables included in the study.

Figure 7: Family History of Bipolar Disorder

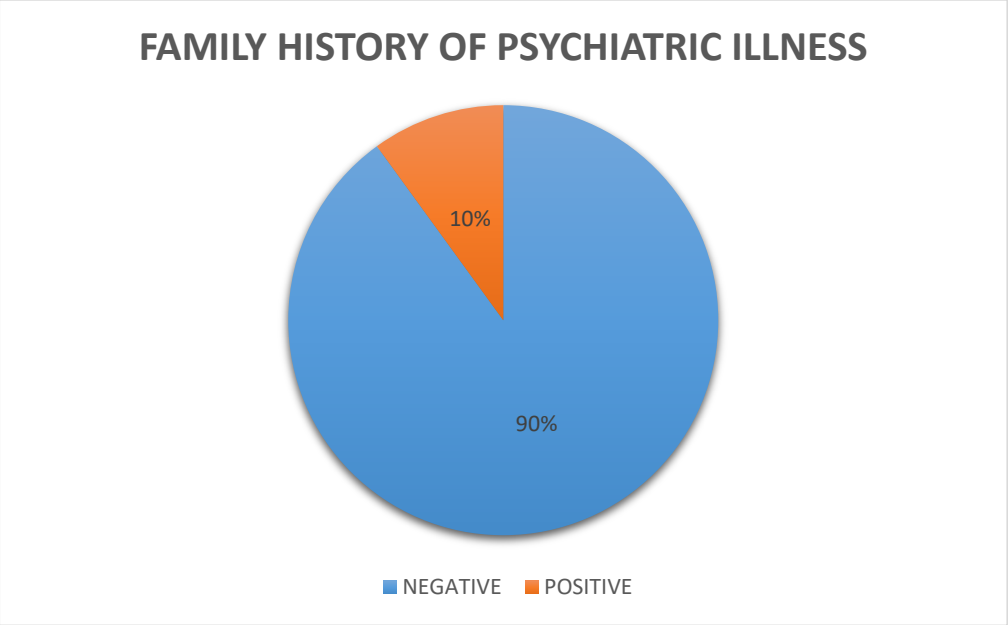

Figure 7 above shows Family History of Psychiatric illness which is positive in 10 % of cases.

Table 8: shows distribution of cases in terms of predominant polarity (N-=100)

PREDOMINANT POLARITY		
	No. of cases	Percentage
Depressive	26	26.00%
Mania	65	65.00%
None	9	9.00%

Figure 8: Predominant Polarity in patients of Bipolar Disorder

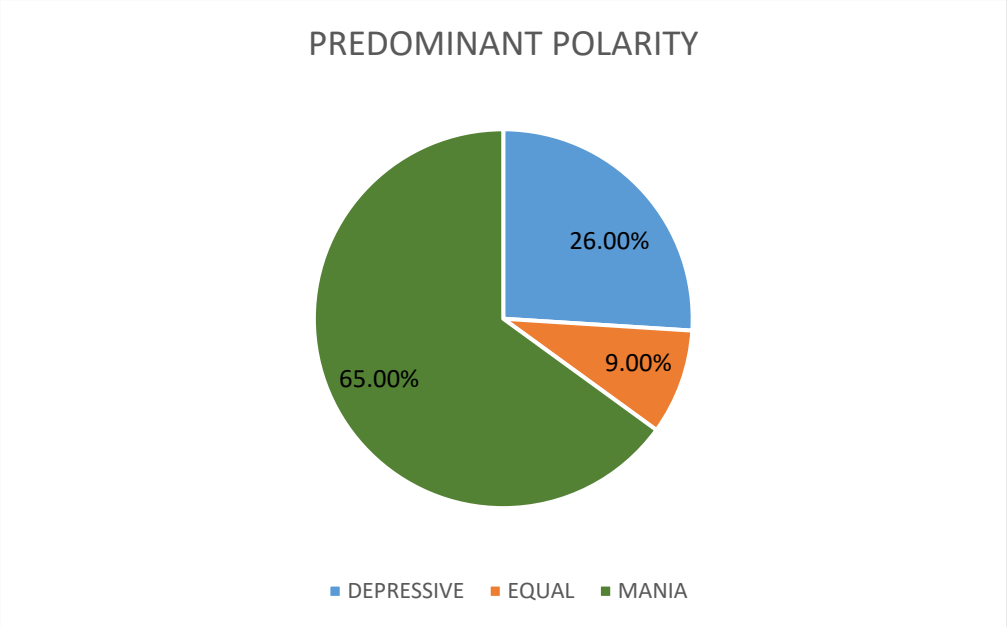

Figure 8 above shows Predominant polarity in patients of bipolar disorder which is manic in 65% , depressive in 26% and none in 9% of the cases.

Table 9: Percentage of Number of manic episodes in patients of bipolar disorder

NO. OF MANIC EPISODES		
	No. of cases	**Percentage**
0	9	9.00%
1	29	29.00%
2	36	36.00%
3	14	14.00%
>3	12	12.00%

Table 9 shows distribution of cases in terms of number of manic episodes a patient had during the entire duration of illness (N-=100)

Figure 9: Percentage of Number of manic episodes in patients of bipolar disorder

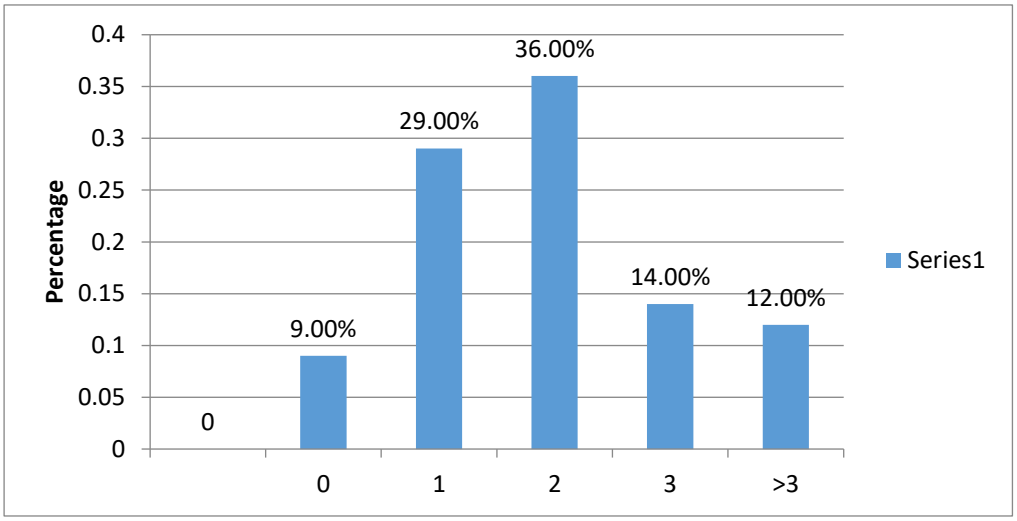

Figure 9 shows the percentage of number of manic episodes the patients of bipolar disorder had during the entire duration of illness. Majority of the patients (I.e. 36%) had 2 episodes of mania followed by 29% having 1 episode, 14% having 3 episodes , 12% having >3 episodes and 9% having no manic episode.

Table 10: Percentage of Number of depressive episodes in patients of bipolar disorder

NO. OF DEPRESSIVE EPISODES		
	No. of cases	**Percentage**
0	32	32.00%
1	32	32.00%
2	23	23.00%
3	8	8.00%
>3	5	5.00%

Table 10 shows distribution of cases in terms of number of depressive episodes a patient had during the entire duration of illness (N=100)

Figure 10: Percentage of Number of depressive episodes in patients of bipolar disorder

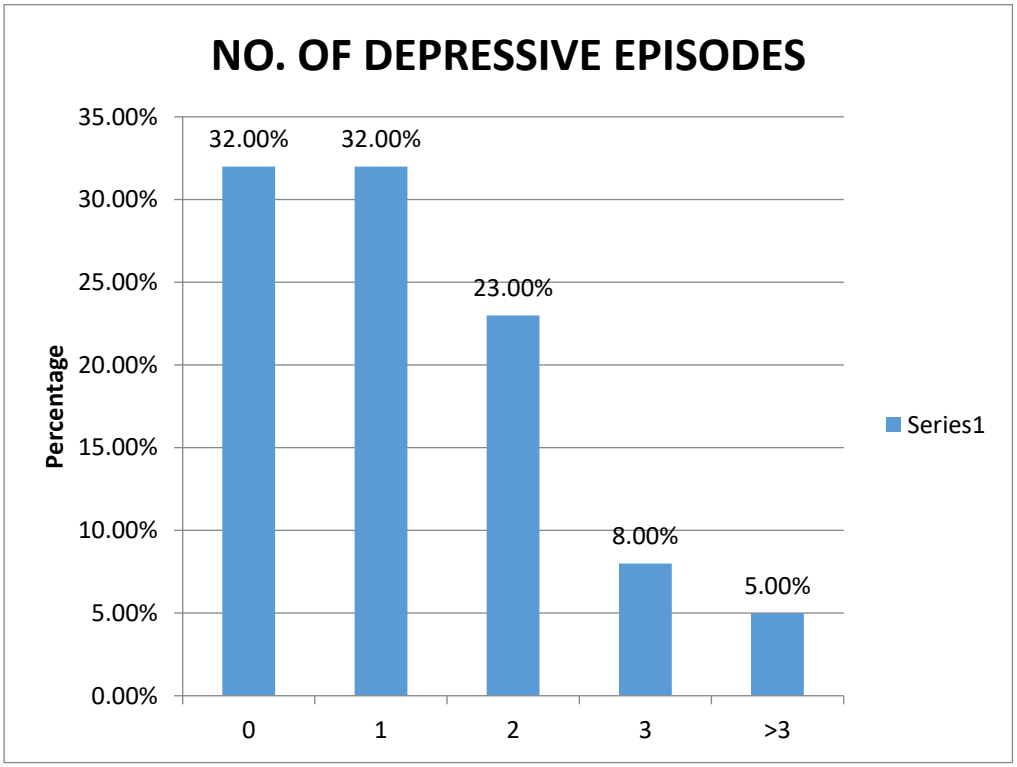

Figure 10 shows the percentage of number of depressive episodes the patients of bipolar disorder had during the entire duration of illness. Majority of the patients (I.e. 32%) had 0-1 depressive episode.

Table 11: Percentage of Number of hospitalisations in patients of bipolar disorder

NO. OF HOSPITALISATIONS		
	No. of cases	**Percentage**
0	52	52.00%
1	30	30.00%
2	14	14.00%
>2	4	4.00%

Table 11: Shows distribution of cases in terms of number of hospitalisations a patient had during the entire duration of illness (N-=100)

Figure 11: Percentage of Number of hospitalisations in patients of bipolar disorder

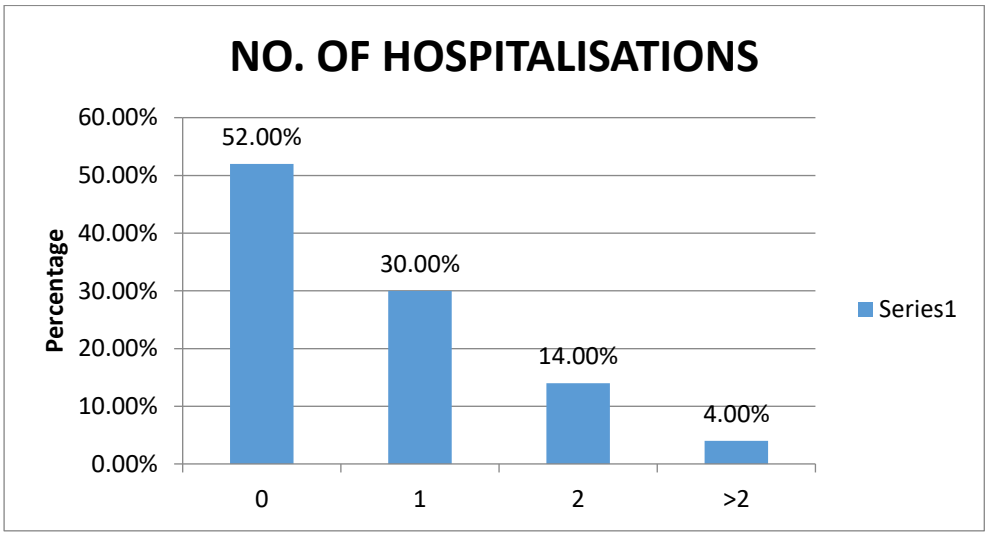

Figure 11 shows the percentage of number of hospitalisations the patients of bipolar disorder had during the entire duration of illness. Majority of the patients (I.e. 52 %) had 0 hospitalisations followed by 1 in 30%, 2 in 14 % and >2 in 4% cases.

Table 12: Type of Mood Stabilisers used in patients of bipolar disorder

MOOD STABILISERS		
	No. of cases	**Percentage**
DIVALPROEX	66	66.00%
LITHIUM CARBONATE	26	26.00%
OXCARBAMAZEPINE	2	2.00%
OLANZAPINE	3	3.00%
RISPERIDONE	3	3.00%

Table 12 shows the type of mood stabilisers the patient was on. (N=100)

Figure 12: Type of Mood Stabilisers used in patients of bipolar disorder

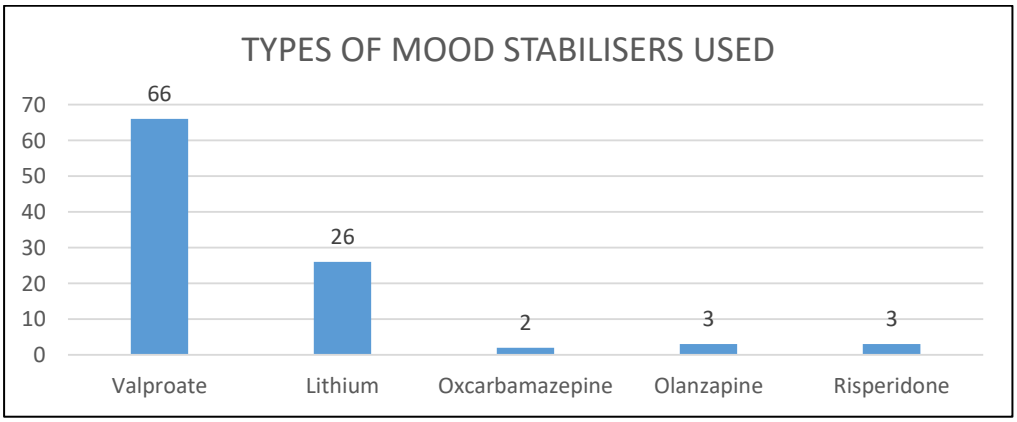

Figure 12 shows the type of mood stabilisers the patients are on. Majority patients were on Divalproex i.e. 66% followed by Lithium Carbonate (26%), Olanzapine (3%), Risperidone (3%), Oxcarbamazepine(2%)

Table 13: below indicates descriptive statistics for the quantitative variables among cases.

Table 13 : Descriptive Statistics for Quantitative variables among cases (N=100)				
Study Parameter	**MIN**	**MAX**	**MEAN**	**SD**
AGE (IN YEARS)	18	66.00	40.52	12.34
DURATION OF ILLNESS(IN YEARS)	2	30.00	7.82	6.84
NO. OF HOSPITALISATIONS	0.00	3.00	0.70	0.86
TOTAL NUMBER OF EPISODES	1	12	3.7	2.04
NUMBER OF MANIC EPISODES	0	8.00	2.09	1.58
NUMBER OF DEPRESSIVE EPISODES	0	5.00	1.24	1.19

Table 13 shows Descriptive Statistics for Quantitative variables among cases. It shows that the mean age of patients of bipolar disorder in our study was 40.52 years (SD=12.34). Mean duration of illness was 7.82 years (SD=6.84). Mean number of hospitalisations was 0.70(SD=0.86). Mean number of manic episodes and depressive episodes were 2.09(SD=1.58) and 1.24(SD=1.19) respectively.

Table 14 below shows the mean value of scores of Indian Disability Evaluation and Assessment Scale (IDEAS)

Table 14: Mean Values of IDEAS among cases (N=100)				
IDEAS	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Self- care	0.00	3.00	0.95	0.90
Interpersonal activities	0.00	3.00	0.98	0.83
Communication and understanding	0.00	2.00	0.89	0.72
Work	0.00	4.00	1.47	0.81
Total score (A)	0.00	10.00	4.26	1.71
Duration of illness score (B)	1.00	4.00	2.54	1.19
Global score (A+B)	2.00	14.00	6.79	2.27

Table 14 shows that the mean value of scores of Indian Disability Evaluation and Assessment Scale (IDEAS). Mean score on IDEAS is 6.79 with Standard deviation of 2.27 which falls within Mild to moderate disability.

Figure 13: Mean values of scores of IDEAS

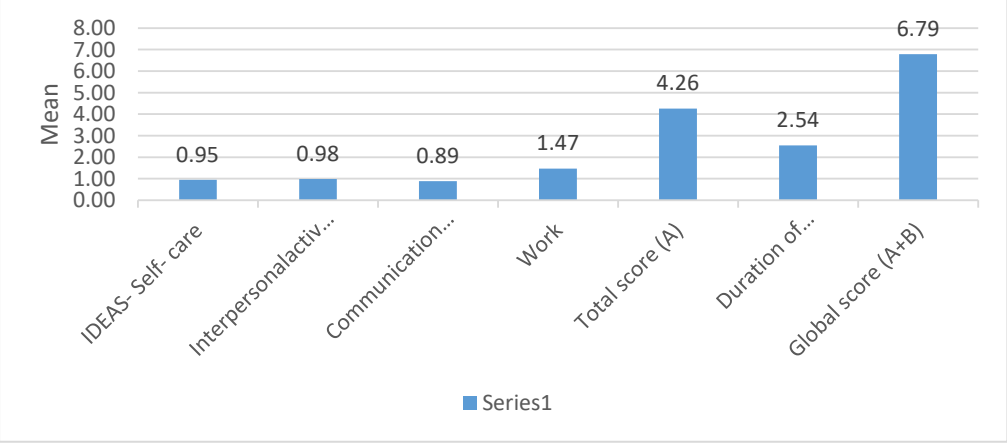

Figure 13 above shows the mean value of scores of Indian Disability Evaluation and Assessment Scale (IDEAS).

Table 15 below shows the comparison of Trail Making Test among cases and controls.

Table 15: Comparison of TRAIL MAKING TEST SCORE A and B between cases and controls						
	Cases(N=100)		Controls(N=50)		t	p-value
	Mean(in seconds)	SD(in seconds)	Mean(in seconds)	SD(in seconds)		
TRAIL MAKING TEST SCORE- A	35.64	10.24	30.42	7.61	3.189	0.002
TRAIL MAKING TEST SCORE- B	78.74	25.59	75.66	21.87	0.728	0.468

Table 15 shows the total mean time taken to complete Trail making test-A, a measure of attention, among cases was 35.64 seconds (SD=10.24) and among controls it was 30.42 seconds (SD=7.61). The time taken to complete the test by cases was more as compared to controls. The result of independent sample t-test indicates a significant difference in the mean trail making test score-A among cases and controls ($t=3.189$, $p < .01$).

The total mean time taken to complete Trail making test-B, a measure of attention, among cases was 78.74 seconds (SD=25.59) and among controls it was 75.66 seconds (SD=21.87). The time taken to complete the test by cases was more as compared to controls. The result of independent sample t-test indicates no significant difference in the mean trail making test score-B among cases and controls ($t=0.728$, $p=0.468$).

Figure 14: Comparison of trail making test-A and B

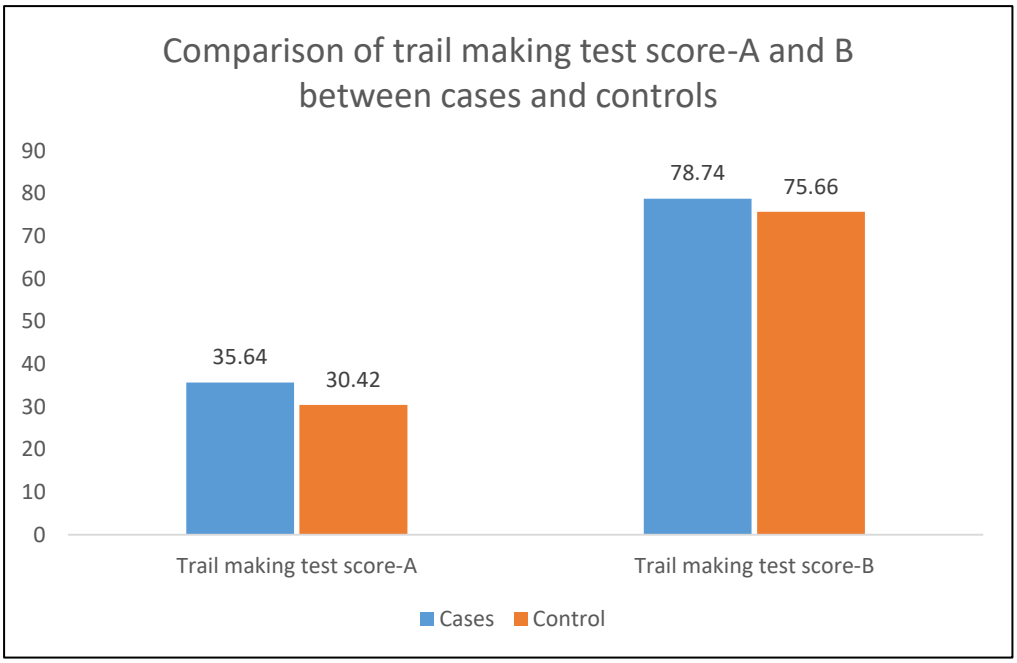

Figure 14 shows comparison of trail making test-A and B among cases and controls.

Table 16 below shows the comparison of Digit Span test among cases and controls.

Table 16 : Comparison of digit forward and digit backward between cases and controls						
	Cases(N=100)		**Controls(N=50)**		t	p-value
	Mean	SD	Mean	SD		
DIGIT FORWARD	4.28	0.88	5.82	1.27	-8.673	0.001
DIGIT BACKWARD	3.63	0.75	4.58	1.03	-6.436	0.001

Table 16 shows the mean digit forward score among cases was 4.28 (SD=0.88) and among controls it was 5.82 (SD=1.27). It indicates that attention was impaired in cases as compared to controls. The result of independent sample t-test indicates a statistically significant difference in the digit forward score among cases and controls (t=-8.673, p=0.001).

The mean digit backward score among cases was 3.63 (SD=0.75) and among controls it was 4.58 (SD=1.03). Digit Backward, a measure of working memory, was better in controls as compared to cases. The result of independent sample t-test indicates a statistically significant difference in the digit backward score among cases and controls (t=-6.436, p =0.001).

Figure 15: Comparison of Digit Span test among cases and controls

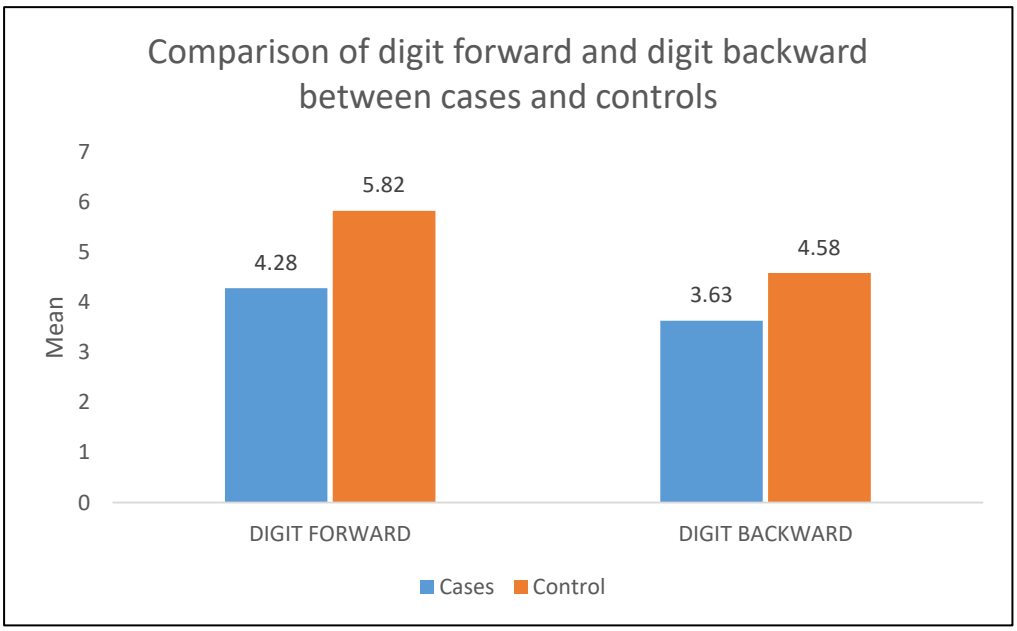

Figure 15 shows the comparison of Digit Span test among cases and controls.

Table 17: below shows the comparison of Digit Symbol Substitution test among cases and controls.

Table 17: Comparison of digit symbol substitution score between cases and controls						
	Cases(N=100)		Controls(N=50)		t	p-value
	Mean	SD	Mean	SD		
DIGIT SYMBOL SUBSTITUTION SCORE	46.88	10.04	68.78	10.83	-12.263	0.001

Table 17 shows the mean digit symbol substitution score among cases was 46.88 (SD=10.04) and among controls it was 68.78 (SD=10.83). This indicates that controls performed better than cases in terms of processing speed. The result of independent sample t-test indicates a statistically significant difference in the digit symbol substitution score among cases and controls (t=-12.263, p =0.001).

Figure 16: Comparison of Digit Symbol Substitution test among cases and controls.

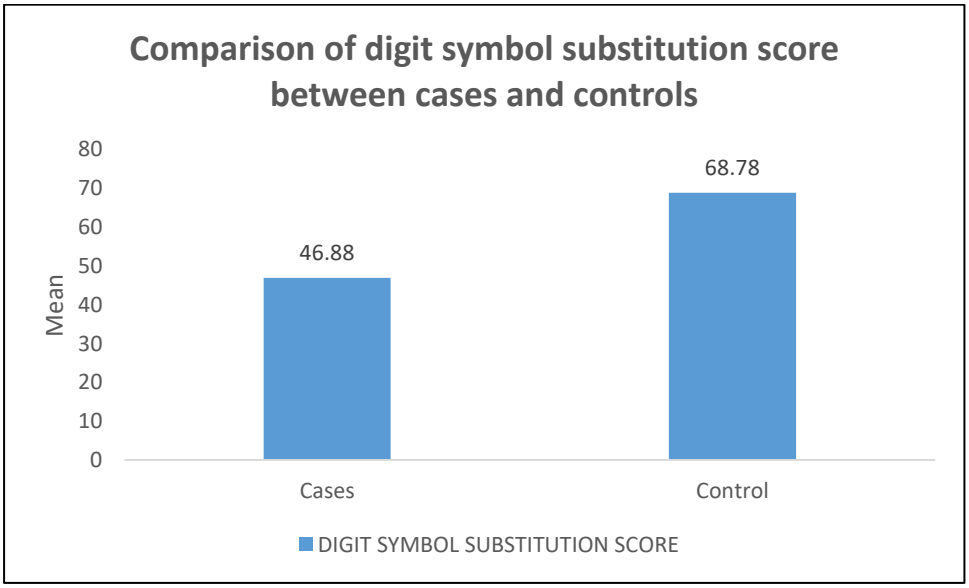

Figure 16 shows the comparison of Digit Symbol Substitution test among cases and controls.

Table 18: shows the comparison of variables of Stroop color word test among cases and controls.

Table 18: Comparison of variables of Stroop color word test among cases and controls						
	Cases (N=100)		Controls (N=50)		t	p-value
	Mean	Sd	Mean	Sd		
STROOP COLOUR TEST SCORE-COLOUR SCORE	63.34	13.55	72.84	9.25	-4.461	0.001
WORD SCORE	73.20	9.03	80.20	12.41	-3.934	0.001
COLOUR-WORD SCORE	46.40	6.78	46.46	6.92	-0.051	0.960
PREDICTED COLOUR WORD	33.38	4.01	37.83	3.98	-6.422	0.001
INTERFERENCE SCORE	13.02	7.98	8.63	7.26	3.273	0.001

Table 18 shows the mean stroop colour test score-colour score among cases was 63.34 (SD=13.5) and among controls it was 72.84 (SD=9.25). It was better in controls as compared to cases. The result of independent sample t-test indicates a statistically significant difference in the stroop colour test score-colour score among cases and controls (t=-4.461, p=0.001).

The mean word score among cases was 73.20 (SD=9.03) and among controls it was 80.20 (SD= 12.41). It was better in controls as compared to cases. The result of independent sample t-test indicates a statistically significant difference in the word score among cases and controls (t=-4.461, p=0.001).

The mean colour-word score among cases was 46.40 (SD=6.78) and among controls it was 46.46 (SD= 6.92). It was better in controls as compared to cases. The result of independent sample t-test indicates no significant difference in the colour-word score among cases and controls (t=-0.051, p=0.960).

The mean predicted colour word score among cases was 33.38 (SD=4.01) and among controls it was 37.38 (SD= 3.98). It was better in controls as compared to cases. The result of independent sample t-test indicates a statistically significant difference in the predicted colour word score among cases and controls (t=-6.422, p=0.001).

The mean interference score among cases was 13.02 (SD=7.98) and among controls it was 8.63 (SD= 7.26). Interference score, a measure of cognitive flexibility and response inhibition, was higher among cases depicting greater difficulty in inhibiting interference. The result of independent sample t-test indicates a statistically significant difference in the interference score among cases and controls (t=3.273, p=0.001).

Figure 17: Comparison of variables of Stroop color word test among cases and controls.

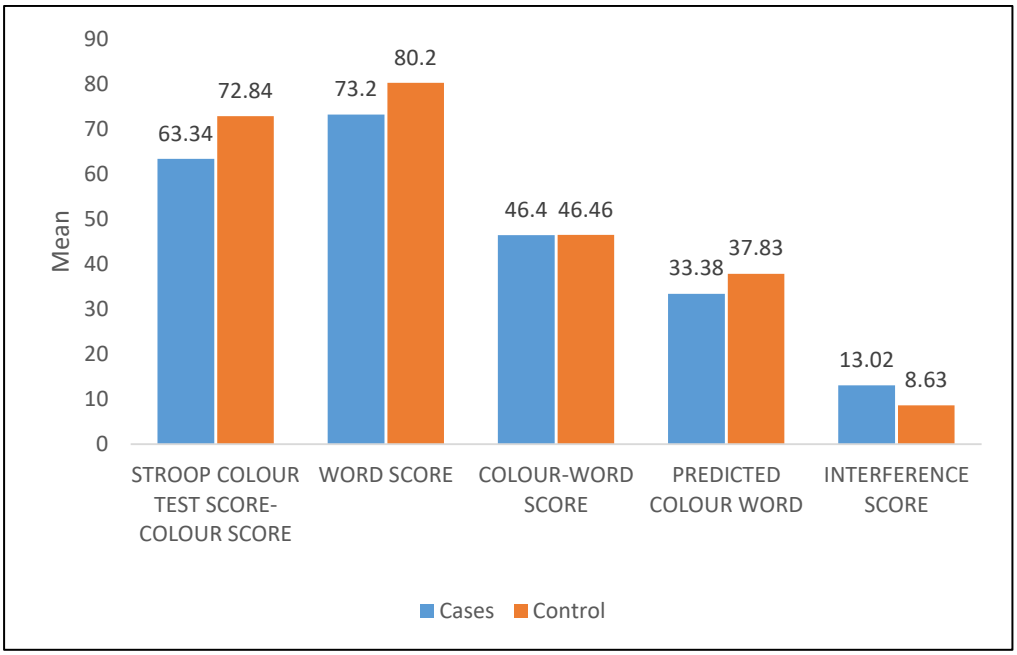

Figure 17 shows the comparison of variables of Stroop color word test among cases and controls.

Table 19: Below shows the comparison of PGI memory test among cases and controls.

Table 19: Comparison of PGI memory test among cases and controls						
	Cases(N=100)		Controls(N=50)		Z	p-value
	Mean	Sd	Mean	Sd		
REMOTE MEMORY	5.50	1.45	5.56	1.20	-0.252	0.801
RECENT MEMORY	4.75	0.63	4.94	0.24	-2.070	0.040
MENTAL BALANCE	7.36	1.59	7.62	1.64	-0.933	0.352
ATTENTION & CONCENTRATION	14.04	4.06	15.02	3.79	-1.424	0.157
DELAYED RECALL	9.36	1.25	9.92	0.34	-3.103	0.002
IMMEDIATE RECALL	11.09	1.33	11.22	0.95	-0.615	0.540
RETENTION FOR SIMILAR PAIRS MEMORY	5.00	0.00	5.00	0.00		
RETENTION FOR DISSIMILAR PAIRS MEMORY	7.73	2.01	8.66	1.30	-2.972	0.003
VISUAL RETENTION	8.93	1.86	8.24	1.45	2.296	0.023
RECOGNITION	9.16	0.44	9.24	0.56	-0.956	0.341
TOTAL SCORE	82.92	5.39	85.42	4.60	-2.807	0.006

Table 19 shows the mean remote memory score among cases was 5.50 (SD=1.45) and among controls it was 5.56 (SD= 1.20). Controls had better remote memory as compared to cases. However, the result indicates no significant difference in the remote memory score among cases and controls (Z=-0.252, p=0.801).

The mean recent memory score among cases was 4.75 (SD= 0.63) and among controls it was 4.94 (SD= 0.24). The performance was better among controls as compared to cases. The result indicates a statistically significant difference in the recent memory score among cases and controls (Z=-2.070, p=0.040).

The mean mental balance score among cases was 7.36 (SD= 1.59) and among controls it was 7.62 (SD= 1.62). The performance was better among controls as compared to cases. The result indicates no significant difference in the mental balance score among cases and controls (Z=-0.933, p=0.352).

The mean attention and concentration score among cases was 14.04 (SD= 4.06) and among controls it was 15.02 (SD= 3.79). It indicates, the attention and concentration was better among controls as

compared to cases. However, the result indicates no significant difference in the attention and concentration score among cases and controls (Z=-1.424, p=0.157).

The mean delayed recall score among cases was 9.36 (SD= 1.25) and among controls it was 9.92(SD= 0.34). It indicates that the controls had better delayed recall than the cases. The result indicates statistically significant difference in the delayed recall score among cases and controls (Z= -3.103, p=0.002).

The mean immediate recall score among cases was 11.09 (SD= 1.33) and among controls it was 11.22 (SD= 0.95). The immediate recall was better among cases as compared to controls. However, the result indicates no significant difference in the immediate recall score among cases and controls (Z=-0.615, p=0.540).

The mean retention for similar pairs memory score among cases was 5.00 (SD= 0.0) and among controls it was 5.00(SD= 0.00). The result indicates no difference in the retention for similar pairs memory score among cases and controls.

The mean retention for dissimilar pairs memory score among cases was 7.73 (SD= 2.01) and among controls it was 8.66 (SD= 1.30). The performance was better among controls as compared to cases. The result indicates statistically significant difference in the retention for dissimilar pairs memory score among cases and controls (Z=-2.972, p=0.003).

The mean visual retention score among cases was 8.93(SD= 1.86) and among controls it was 8.24(SD= 1.45). The visual retention was found to be better among cases than the controls. The result indicates a statistically significant difference in the visual score among cases and controls (Z=2.296, p=0.023).

The mean recognition score among cases was 9.16(SD= 0.44) and among controls it was 9.24(SD= 0.56). Recognition score was better among controls as compared to cases. The result indicates no significant difference in the recognition score among cases and controls (Z=-0.956, p=0.341).

The results of domains Recent memory, delayed recall, retention for similar pairs had significant difference among cases and controls with controls performing better than cases(p= 0.040, 0.002, 0.003, respectively)

The mean total score among cases was 82.92(SD= 5.39) and among controls it was 85.42(SD= 4.60). Both fell in category of Average/Moderate Memory. The result indicates a statistically significant difference in the total score among cases and controls (Z=-2.807, p=0.006).

Figure 18: Comparison of variables of PGI memory test among cases and controls

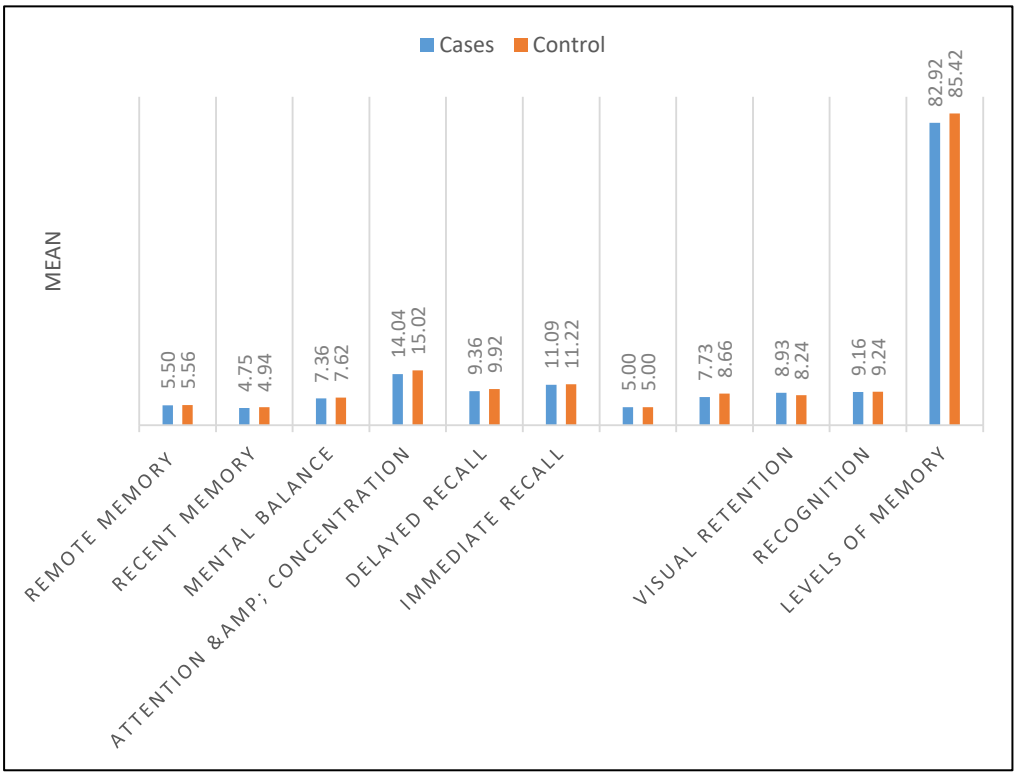

Figure 18 shows the comparison of PGI memory test among cases and controls.

Table 20: Below shows the comparison of mean scores of Trail Making test among various mood stabilisers in patients of bipolar disorder

Table 20 : Comparison of Mean Trail Making Test Score- A and Trail Making Test Score- B among various mood stabilisers						
NEUROPSYCHOLOGICAL TEST	**MOOD STABILISERS**	**NUMBER OF PATIENTS**	**MEAN (in seconds)**	**SD**	**F-stat**	**p-value**
TRAIL MAKING TEST SCORE- A	**LITHIUM CARBONATE**	26	35.7	11.79	4.61	0.011*
	DIVALPROEX	116	32.9	8.97		
	OTHERS	8	42.8	9.054		
TRAIL MAKING TEST SCORE- B	**LITHIUM CARBONATE**	26	79.7	26.61	0.32	0.726
	DIVALPROEX	116	77.7	24.49		
	OTHERS	8	71.8	14.79		

Table 20 shows the mean trail making test score-A among Lithium carbonate, Divalproex and others was 35.7 (SD=11.79), 32.9 (SD=8.97) and 42.8 (SD=9.054) respectively. The time taken to complete the TMT-A was higher in patients receiving Lithium carbonate as compared to other mood stabilisers. The mean Trail Making Test Score- A was found to be significantly worse in patients receiving lithium carbonate as compared to Divalproex and Others ($F=4.61$, $p<.05$).

The mean trail making test score-B among lithium carbonate, Divalproex and others was 79.7 (SD=26.61), 77.7 (SD=24.49) and 71.8 (SD=14.79) respectively. The time taken to complete the TMT-B was higher in patients receiving Lithium carbonate as compared to other mood stabilisers. The mean Trail Making Test Score- B was found to be not significantly different according to Lithium carbonate, Divalproex and Others ($F=0.32$, $p=0.726$).

Figure 19: Comparison of mean scores of Trail Making test among various mood stabilisers in patients of bipolar disorder

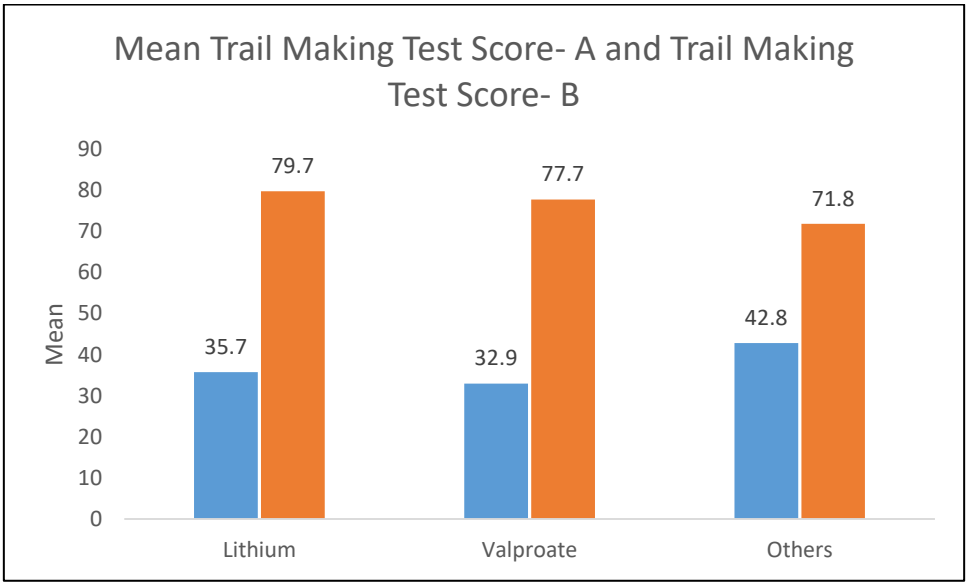

Figure 19 shows the comparison of mean scores of Trail Making test among various mood stabilisers in patients of bipolar disorder

Table 21: Below shows the comparison of mean scores of Digit Span test among various mood stabilisers in patients of bipolar disorder.

Table 21: Comparison of Mean Digit Forward and Digit Backward scores among various mood stabilisers						
NEUROPSYCHOLOGICAL TEST	**MOOD STABILISERS**	**NUMBER OF PATIENTS**	**Mean**	**SD**	**F-stat**	**p-value**
DIGIT FORWARD	**LITHIUM CARBONATE**	26	4.27	0.874	5.24	0.006**
	DIVALPROEX	116	4.97	1.292		
	OTHERS	8	4	1.069		
DIGIT BACKWARD	**LITHIUM CARBONATE**	26	3.58	0.758	3.73	0.026*
	DIVALPROEX	116	4.06	0.989		
	OTHERS	8	3.5	0.756		

Table 21 shows the mean digit forward score among lithium carbonate, Divalproex and others was 4.27 (SD=0.87), 4.97 (SD=1.292) and 4.00 (SD=1.069) respectively. Other mood stabilisers performed worst on Digit Forward as compared to Lithium carbonate and Divalproex treated patients. The mean digit forward score was found to be statistically significantly different according to lithium carbonate, Divalproex and Others (F=5.24, p=0.006).

The mean digit backward score among lithium carbonate, Divalproex and others was 3.58 (SD=0.758), 4.06 (SD=0.989) and 3.50 (SD=0.756) respectively. Other mood stabilisers performed worst on Digit Backward as compared to Lithium carbonate and Divalproex treated patients. The mean digit backward Score was found to be significantly different according to lithium carbonate, Divalproex and Others (F=3.73, p=0.026).

Figure 20 : Comparison of mean scores of Digit Span test among various mood stabilisers in patients of bipolar disorder

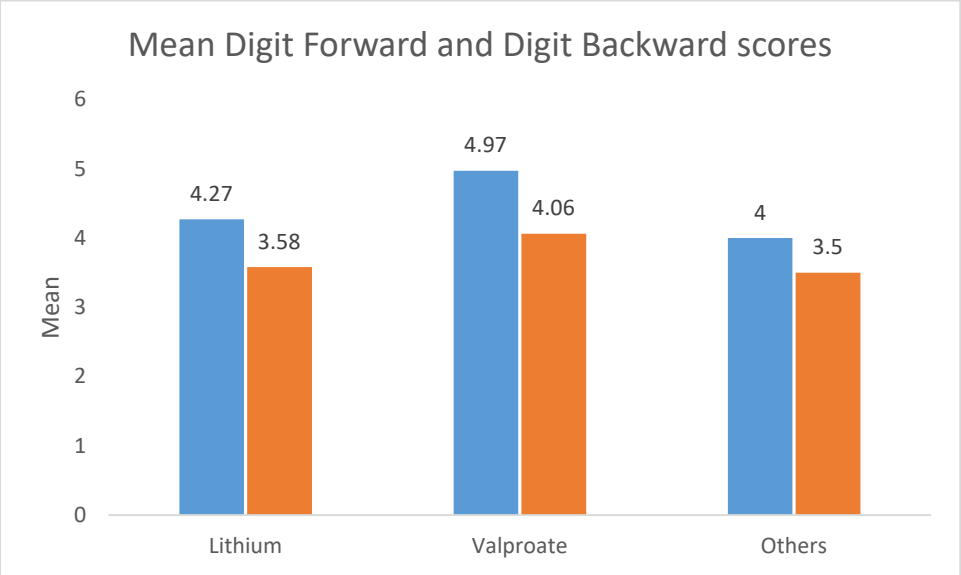

Figure 20 shows the comparison of mean scores of Digit Span test among various mood stabilisers in patients of bipolar disorder.

Table 22: Below shows the comparison of mean scores of DSST among various mood stabilisers in patients of bipolar disorder.

Table 22: Comparison of Mean Digit Symbol Substitution Score among various mood stabilisers						
NEUROPSYCHOLOGICAL TEST	**MOOD STABILISERS**	**NUMBER OF PATIENTS**	**Mean**	**SD**	**F-stat**	**p-value**
DIGIT SYMBOL SUBSTITUTION SCORE	**LITHIUM CARBONATE**	26	44.8	10.09	8.99	0.001**
	DIVALPROEX	116	56.8	14.77		
	OTHERS	8	47.1	9.508		

Table 22 shows the mean Digit Symbol Substitution Score among lithium carbonate, Divalproex and others was 44.8 (SD=10.09), 56.8 (SD=14.77) and 47.1 (SD=9.508) respectively. It indicates that the processing speed measures were worse in Divalproex as compared to other mood stabilisers. The mean digit forward score was found to be statistically significantly different according to Lithium carbonate, Divalproex and Others (F=8.99, p=0.001).

Figure 21 : Comparison of mean scores of DSST among various mood stabilisers in patients of bipolar disorder

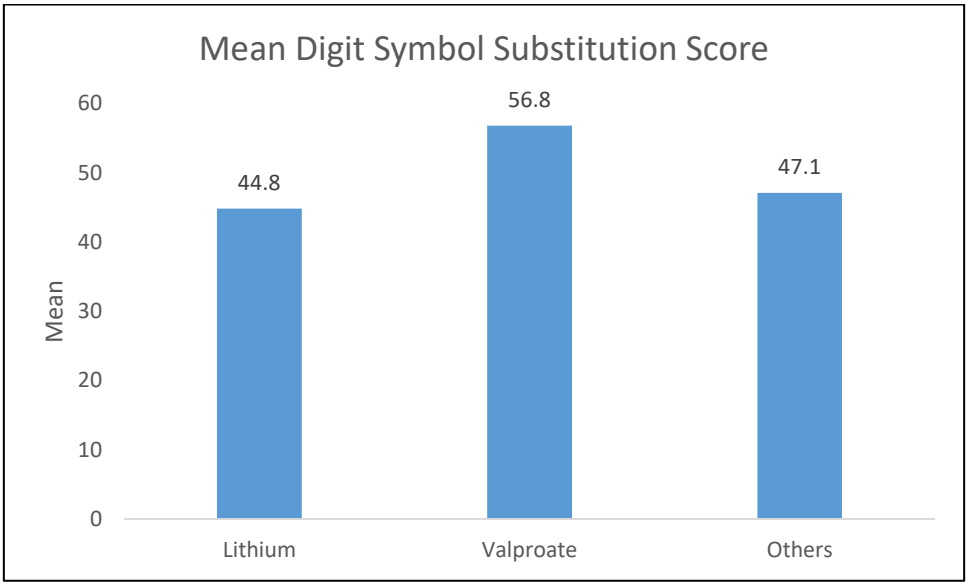

Figure 21 shows the comparison of mean scores of DSST among various mood stabilisers in patients of bipolar disorder.

Table 23: Below shows the comparison of mean scores of SCWT-Interference score among various mood stabilisers in patients of bipolar disorder

Table 23: Comparison of Mean Interference Score among various mood stabilisers						
NEUROPSYCHOLOGICAL TEST	**MOOD STABILISERS**	**NUMBER OF PATIENTS**	**Mean**	**SD**	**F-stat**	**p-value**
INTERFERENCE SCORE	**LITHIUM CARBONATE**	26	14.8	8.769	2.82	0.063
	DIVALPROEX	116	10.8	7.793		
	OTHERS	8	12.6	6.195		

Table 23 shows the Mean Interference Score among Lithium carbonate, Divalproex and others was 14.8 (SD=8.769), 10.8 (SD=7.793) and 12.6 (SD=6.195) respectively. The scores were highest among Lithium carbonate treated patients as compared to other mood stabilisers which denotes greater difficulty in inhibiting interference and poorer cognitive flexbility The Mean Interference Score was found to be not significantly different according to Lithium carbonate, Divalproex and Others (F=2.82, p=0.063).

Figure 22 : Comparison of mean scores of SCWT-Interference score among various mood stabilisers in patients of bipolar disorder

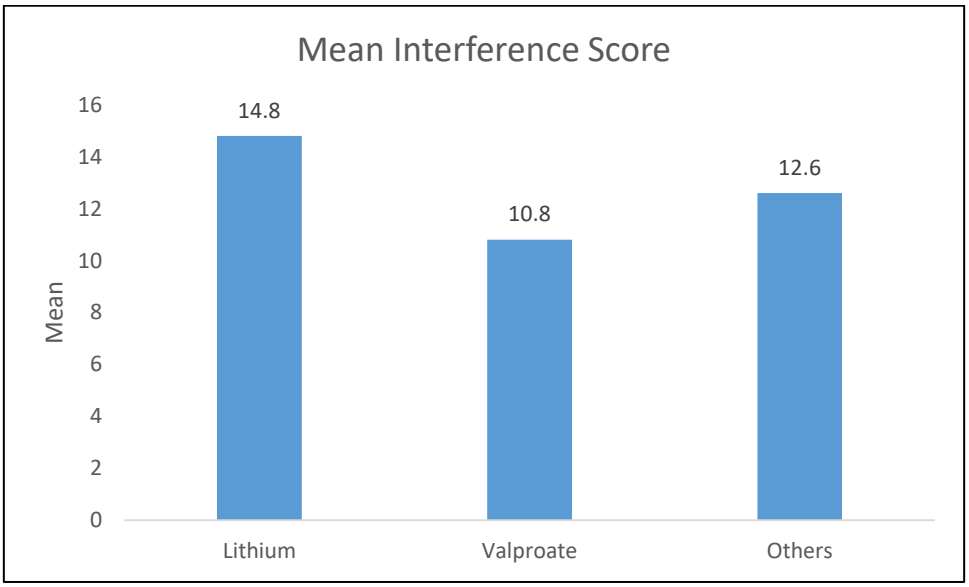

Figure 22 shows the comparison of mean scores of SCWT-Interference score among various mood stabilisers in patients of bipolar disorder

Table 24: Below shows the comparison of Total score of PGI Memory Scale among various mood stabilisers in patients of bipolar disorder

Table 24: Comparison of Total score of PGI Memory Scale among various mood stabilisers						
NEUROPSYCHOLOGICAL TEST	**MOOD STABILISERS**	**NUMBER OF PATIENTS**	**Mean**	**SD**	**F-stat**	**p-value**
TOTAL SCORE OF PGI MEMORY SCALE	**LITHIUM CARBONATE**	26	82.92	5.169	0.999	0.372
	DIVALPROEX	66	83.23	5.176		
	OTHERS	8	80.38	7.633		

Table 24 shows that the mean total score of PGI memory scale among Lithium carbonate, Divalproex and others was 82.92(SD=5.169), 83.23(SD=5.176) and 80.38(SD=7.633) respectively. Other mood stabilisers including Carbamazepine, Olanzapine and Risperidone performed worst followed by Lithium carbonate and then Divalproex treated patients. The mean total score of PGI memory scale was found to be not significantly different according to lithium carbonate, Divalproex and Others (F=0.999, p=0.372).

Figure 23: Comparison of Total score of PGI Memory Scale among various mood stabilisers in patients of bipolar disorder

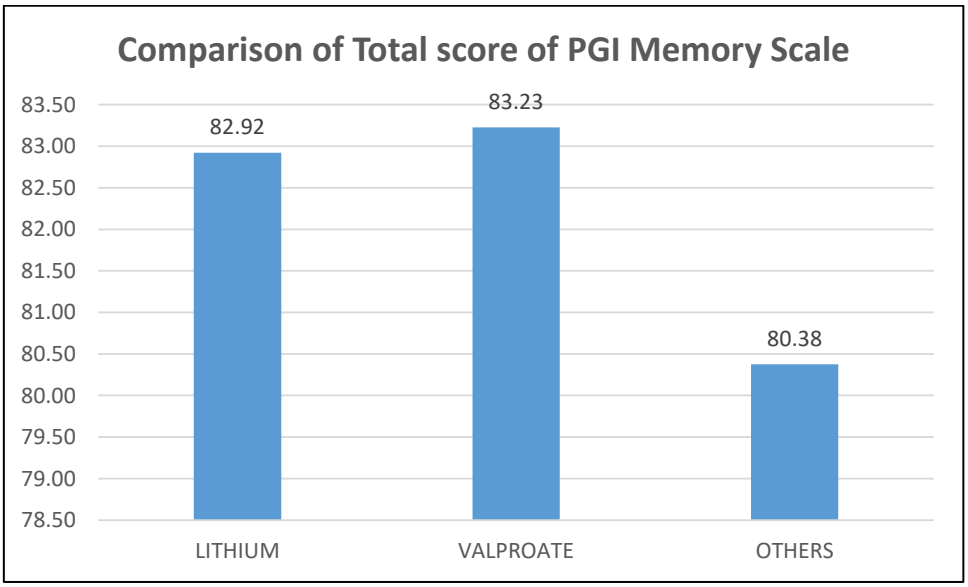

Figure 23 shows the comparison of Total score of PGI Memory Scale among various mood stabilisers in patients of bipolar disorder

Table 25: Below shows the comparison of mean Global scores of IDEAS among various mood stabilisers in patients of bipolar disorder

Table 25: Comparison of Mean IDEAS Global score (A+B)						
NEUROPSYCHOLOGICAL TEST	**MOOD STABILISERS**	**Number of patients**	**Mean**	**SD**	**F-stat**	**p-value**
IDEAS GLOBAL SCORE (A+B)	**LITHIUM CARBONATE**	26	6.31	2.346	0.8	0.454
	DIVALPROEX	66	6.97	2.148		
	OTHERS	8	6.88	3.044		

Table 25 shows that the Mean IDEAS Global score (A+B) among lithium carbonate, Divalproex and others was 6.31 (SD=2.346), 6.97 (SD=2.148) and 6.88 (SD=3.044) respectively. It shows that disability scores were worst among Divalproex treated individuals followed by Other mood stabilisers and then Lithium carbonate. The Mean IDEAS Global score (A+B) was found to be not significantly different according to lithium carbonate, Divalproex and Others (F=0.800, p=0.454).

Figure 24 : Comparison of mean Global scores of IDEAS among various mood stabilisers in patients of bipolar disorder

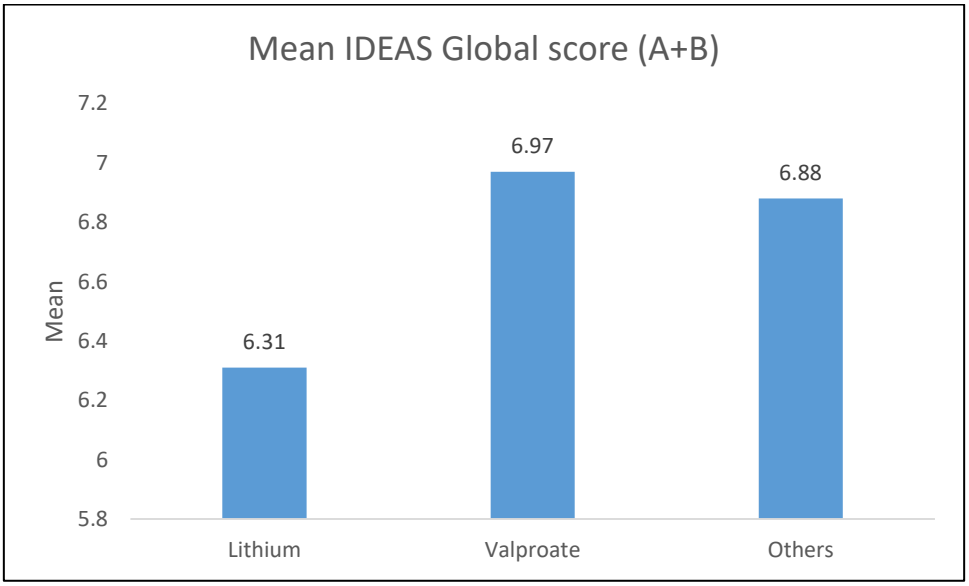

Figure 24 shows the comparison of mean Global scores of IDEAS among various mood stabilisers in patients of bipolar disorder

Table 26: Below indicates correlation of neuropsychological tests and Global score of IDEAS with Age of the patient of bipolar disorder (N=100).

Spearman's rho		TRAIL MAKING TEST SCORE-A	TRAIL MAKING TEST SCORE-B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	INTERFERENCE SCORE	LEVELS OF MEMORY	Global score (A+B)
AGE	Correlation Coefficient	-0.028	0.018	-0.058	-0.006	-0.089	0.049	0.036	0.190
	p-value	0.782	0.859	0.570	0.951	0.376	0.627	0.721	0.058

Table 26 shows that the age of the patient of bipolar disorder is negatively associated with TMT-A, Digit Forward, Digit Backward and DSST whereas it is positively associated with TMT-B, Interference score of SCWT, level of memory and Global score of IDEAS. It suggests that with increasing age of the patient, there was worse performance on all tests except TMT-A and PGI-memory scale. However, none of the results were statistically significant.

Table 27: Below indicates correlation of neuropsychological tests and Global score of IDEAS with Duration of illness in the patient of bipolar disorder (N=100).

Spearman's rho		TRAIL MAKING TEST SCORE-A	TRAIL MAKING TEST SCORE-B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	SCWT-INTERFERENCE SCORE	LEVELS OF MEMORY	Global score (A+B)
DURATION OF ILLNESS	Correlation Coefficient	-0.047	-0.089	0.145	-0.126	0.015	0.049	0.154	0.685
	p-value	0.643	0.377	0.149	0.210	0.882	0.629	0.127	0.000

Table 27 shows that the duration of illness is negatively associated with TMT and Digit Backward. It is positively associated with Digit forward, DSST, SCWT-interference score and level of memory. With increasing duration of illness, there was worse performance on all tests except TMT, Digit Forward, DSST and PGI-memory scale. But these results were insignificant.

The duration of illness (in years) was significantly positively associated with the global score of IDEAS. (p=0.00). It indicates that with increasing duration of illness among cases, the disability scores increased.

Table 28: Below indicates correlation of neuropsychological tests and Global score of IDEAS with Total number of episodes in the patients of bipolar disorder (N=100).

Spearman's rho		TRAIL MAKING TEST SCORE-A	TRAIL MAKING TEST SCORE-B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	SCWT-INTERFERENCE SCORE	LEVELS OF MEMORY	Global score (A+B)
TOTAL NO. OF EPISODES	Correlation Coefficient	0.128	-0.028	-0.419	-0.370	-0.527	0.218	0.231	0.585
	p-value	0.118	0.733	0.000	0.000	0.000	0.007	0.004	0.000

Table 28 shows that the Total number of episodes was significantly negatively associated with the variables Digit Forward, Digit Backward, Digit Symbol Substitution Score, SCWT-Interference Score.($p<.01$). Total episodes was significantly positively associated with the study variables Interference Score, Levels of Memory, Colour-Word Score, and Global Score (A+B) ($p<.01$). It indicates that with increase in total No. of episodes, performance was worse on all the scales except TMT-A and the disability score worsens.

Table 29: Below indicates correlation of neuropsychological tests and Global score of IDEAS with Total number Manic episodes in the patients of bipolar disorder (N=100).

Spearman's rho	n=100	TRAIL MAKING TEST SCORE-A	TRAIL MAKING TEST SCORE-B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	INTERFERENCE SCORE	LEVELS OF MEMORY	Global score (A+B)
NO. OF MANIC EPISODES	Correlation Coefficient	-0.160	-0.071	0.175	-0.031	0.139	-0.005	-0.061	0.469
	p-value	0.113	0.481	0.082	0.761	0.166	0.960	0.549	0.001

Table 29 shows that the total number of manic episodes was negatively associated with TMT-A, TMT-B, Digit Backward, interference score and level of memory. It was positively associated with Digit Forward, DSST and Global score of IDEAS. It indicates that with increase in total number of manic episodes, performance is worse on Digit Backward, DSST, PGI memory and better on other scales. However, it is not statistically significant. Total no. of manic episodes is significantly positively associated with Global score of ideas. (p=0.001). It indicates that with increasing Number of manic episodes among cases, the disability scores increased.

Table 30: Below indicates correlation of neuropsychological tests and Global score of IDEAS with Total number of Depressive episodes in the patients of bipolar disorder (N=100).

Spearman's rho	n=100	TRAIL MAKING TEST SCORE-A	TRAIL MAKING TEST SCORE-B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	INTERFERENCE SCORE	LEVELS OF MEMORY	Global score (A+B)
NO. OF DEPRESSIVE EPISODES	Correlation Coefficient	-0.003	-0.165	-0.009	-0.077	0.019	0.021	-0.001	0.123
	p-value	0.976	0.100	0.928	0.445	0.853	0.838	0.992	0.225

Table 30 shows that the total number of depressive episodes was negatively associated with TMT-A, TMT-B, Digit Forward and level of memory. It was positively associated with Digit Backward, DSST , SCWT-interference score and Global score of IDEAS. It indicates that with increase in total number of depressive episodes, performance is worse on Digit Forward, PGI memory , SCWT and better on other scales. However, it is not statistically significant.

Table 31: Below indicates correlation of neuropsychological tests and Global score of IDEAS with Total number of Hospitalisations in the patients of bipolar disorder (N=100).

Spearman's rho		TRAIL MAKING TEST SCORE-A	TRAIL MAKING TEST SCORE-B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	SCWT-INTERFERENCE SCORE	LEVELS OF MEMORY	Global score (A+B)
NO. OF HOSPITALISATIONS	Correlation Coefficient	-0.049	-0.151	0.007	0.031	0.154	-0.042	-0.164	0.233
	p-value	0.629	0.135	0.942	0.757	0.126	0.678	0.104	0.020

Table 31 shows that the total number of hospitalisations was negatively associated with TMT-A, TMT-B, SCWT-Interference and Level of memory. It was positively associated with Digit Forward, Digit Backward, DSST and Global score of IDEAS. It indicates that with increasing number of hospitalisations, there is worse performance on all tests except ? SCWT and TMT. The number of Hospitalisations was statistically significantly positively associated with the Global score (A+B) (p=0.020). It indicates increase in Disability scores with increased number of Hospitalisation.

DISCUSSION

The bipolar disorder is a chronic disorder with a high recurrence rate, significant general disability and psychosocial impairment. The cognitive impairment is often considered as a basic characteristic of bipolar disorder. Available evidence depicts that cognitive dysfunction is a critical mediator of adverse psychosocial outcomes in BD and a predictor of unfavorable employment outcomes. It is worth mentioning that cognitive impairment needs to be considered a therapeutic clinical target in order to improve both psychosocial functioning and quality of life of patients with BD. The main aim of our study was to assess the cognitive functions in bipolar patients. The study was conducted on 100 patients in age group 18-65 years diagnosed as Bipolar Disorder in remission presented to the Department of Psychiatry, DMC&H Ludhiana and 50 healthy controls in age group 18-65 years which investigated the cognitive performance of patients with bipolar disorder compared with healthy control subjects during a well-established euthymic mood.

Numerous studies have established that the cognitive parameters including verbal memory, attention, and executive skills are all compromised in bipolar disorder patients [(51)]. A study done by **Ferrier et al (1999)** [(34)] included patients with euthymic bipolar disorder and showed impairment of executive function as compared to healthy controls. A systematic review of the computerized literature of neuropsychological studies of BD published between 1980 and 2000 was conducted by **Quraishi S et al (2002)** [[40]] which showed impairment in attention**,** executive function and verbal memory with variable results on visuo-spatial memory deficits depending on the tasks used. Similar findings were observed by **Savitz J et al** [[29]] in 2005 with bipolar patients having deficit of attention, learning and memory, and executive function. Our study corroborates these findings and showed that the cognitive performance was significantly lower as compared to healthy controls particularly with respect to attention, memory, processing speed and executive functions. Compared to

healthy controls, euthymic bipolar individuals exhibited clinically substantial cognitive impairments.

There was no significant difference between the two groups in terms of distribution of age. The mean age of the remission cases was 40.52 ± 12.34 years, which was similar to that of 42 ± 2 years obtained in a study by **Rubinsztein et al.** [38]**. Braw et al** [52] observed a mean age of 39.07 (±13.68) years in the bipolar disorder remission cases. Majority of the cases were males (80%). Similar male predilection in cases was also seen in a study by **Braw et al.** [52]

Most of the cases were skilled workers (44%) and unemployed (32%). Unemployment can be due to socio-occupational dysfunction caused by the illness. In a study by **Verma et al**[53], it was observed that 36.67% cases had clerical jobs. Majority of the patients (74%) and healthy controls (82%) were married as can be expected from the age group of patients taken. Similar results were obtained by **Verma et al**[53] with 83.33% cases and 80% controls being married.

A family history of psychiatric illness was present in 10 % of cases which was less as that observed by **Zhong et al** [54] who saw 25.45% cases showing a family history of psychiatric illness.

In our study, 65% patients showed manic polarity followed by depressive in 26% and indeterminate in 9% of the cases. Studies from the tropics suggest a significantly higher incidence of mania in the course of BD. As seen in previous studies by Chopra et. Al [55], manic episodes accounted for 72% of all the episodes in a study from India.

Contrary to the general observation that patients with BD experience more of depression than mania, some of the studies from India [55,56,57] (Chopra et al., 2006; Khanna et al., 1992; Khess et al., 1997), Nigeria [58] (Makanjuola, 1985), Ethiopia[59] (Fekadu et al., 2006), Israel[60] (Osher et al., 2000) and Hong Kong[61] (Lee, 1992) report that mania constitutes a greater part of BD course than depression. Our study confirms this observation. One can only speculate the potential mediating effect of genetic differences and environmental factors such as sunlight and latitude in determining the predominant course. BD has

a strong genetic component and it has been recognized increasingly that circadian rhythm abnormalities could play an important role in the recurrence and symptom expression. For instance, variations in the CLOCK gene suggest that CLOCK3111 T/C C/C allele is associated with a higher recurrence rate [62] (Benedetti et al., 2003). A CLOCK mutant mouse might constitute an animal model of mania[63] (Roybal et al., 2007). Apart from these possible genetic differences, variations in sunlight can also play a role [64] (Bauer et al., 2015). The countries where mania is predominant are from lower latitudes where ambient sunlight is greater. Indeed, such epigenetic influences affecting circadian rhythm have been implicated in disease states [65] (Masri and Sassone-Corsi, 2013).

During the entire duration of illness, 48% patients were hospitalized during the acute phase with 4% patients having more than 2 hospitalizations. The mean number of hospitalizations was 0.70 **±**0.86 which was lower than that observed by **Braw et al** [52] i.e. 2.68 ±1.91. This observation can be because of younger sample of population in our study.

Mean score on IDEAS is 6.79 ± 2.27 which falls within Mild to moderate disability. Our study found that all domains of functioning were affected especially work and interpersonal relations. The Indian study by **Chaudhury et al.** [66] and other studies [67] using IDEAS also found that all the core domains of functioning, i.e., self-care, interpersonal relations, communication and work are affected in BD patients and interpersonal relations is the area affected the most.

In our study, there was a correlation between disability and age group indicating that disability increased with increasing age but it was not statistically significant which is in contrast with the Indian study done by **Thomas *et al*.** [68]However, Mixed-Effects Modeling research done on USA and European populations by **Bennett *et* al. [69]** did not find any association between age and gender with the functional outcome in a longitudinal study to assess the functional outcome using GAF

score. This variation could be due to the use of a different methodological design of the study.

In our study, mean duration of illness is 7.82 years (SD=6.84). In a study by **Braw et al** [52], the mean duration of illness was seen to be 13.29 (±12.32) years while **Gruber et al** [70] noted it to be 26.2 ± 2.9 days.

The statistical significance was found between duration of illness and disability which is in concurrence to the earlier studies done by **Chacko D et al. and Tohen M. et al.**[71,72] Our study found a statistically significant association between total number of episodes and disability, which is in concurrence to the earlier studies done by **Chacko D et al and Jiménez et al.**[71,72] This highlights that the recurrent course of BD is associated with more disability. There was statistically significant association between repeated previous hospitalizations and overall psychosocial impairment, which is in line with the previous studies done by **Jiménez *et al*.**[73]

There was a highly significant difference in the mean TMT-A score, a test of attention, visual screening ability, and processing speed, among cases (35.64 ± 10.24) and controls (30.42 ± 7.61). However, in case of TMT-B, which has an additional requirement of maintaining and shifting of mental set, score, although the score in cases (78.74 ± 25.59) was higher than that in the controls (75.66 ± 21.87) which means they took more time to complete the test and performed worse than control subjects but it was not significant. Similar results of a higher score in the bipolar group was also seen in a study by **Gruber et al**[70] with the score in and being 44.0 ± 14.2 and 64.8 ± 28.1 respectively. In a study by **Pradhan et al**[74], The mean TMT-B score in bipolar group was 132.42 ± 8.79 while in the control it was 103.44 ± 15.63. It denotes impaired attention and executive functions in bipolar disorder.

The mean digit forward score among cases (4.28 ± 0.88) was lower when compared to the controls (5.82 ± 1.27). Similarly, the mean digit backward score among cases (3.63 ± 0.75) was lower than of controls

(4.58 ± 1.03). This was in concordance to results obtained by Verma et al who noted that the mean Digit span forward test comparison between patient groups and the healthy control group (4.33 ± 0.66 and 5.03 ± 0.71) was statistically significant. In our study, after controlling for age, the bipolar patients had a worse performance than the control group on working memory measures (Digit Span Backwards) and attention (TMT part A and Digit Span Forwards). Ferrier et al. (34) concluded that a deficit of working memory was observed in remitted bipolar patients and suggested that their findings may reflect frontal lobe damage or disruption of fronto-subcortical or mesolimbic circuitry.

The mean DSST score, a measure of psychomotor speed, among cases (46.88 ± 10.04) was lower than of controls (68.78 ± 10.83). Similar results were obtained by **Zhong et al.** [54]

Our results for executive function measures presented a two dimensional feature: impaired performance on selective attention and inhibitory control (on SCWT). The SCWT is considered as more specifically focused on attentional domain, especially owing to time pressure. The mean stroop colour test score-colour score among cases was lower than those of controls as was seen with word score and the colour-word score. It depicted that bipolar patients read less words in the similar time allotted than our control subjects. The mean predicted colour word score among cases was 33.38 ± 4.01 while that in the controls it was 37.38 ± 3.98. The mean interference score was 13.02 ± 7.98 and 8.63 ± 7.26 among cases and controls respectively. On the Stroop Color Word Test, bipolar patients performed significantly slower on all three conditions (Color Naming, Word Reading, and Interference) relative to control subjects. a lower score means greater difficulty in inhibiting interference. The test is essentially a measure of cognitive flexibility and response inhibition. Thus, patient of bipolar disorder performed worse on executive functions than controls.

Contrasting results were obtained in a study by **Gruber et al**[70], wherein higher scores were obtained for the cases when compared with the controls. The interference score was positively associated with

the total number of episodes which is in concurrence to our study as shown in Table 29. (p=0.007) These findings support recent bipolar patient neuroimaging studies that show changes in frontal areas (75,76). In bipolar patients, structural MR studies have shown changes in subregion-specific prefrontal volume[80], and declines in frontal activity during cognitive challenge tasks on several functional imaging studies [77,78,79]

When performing the interference condition of the Stroop test, bipolar patients showed significantly reduced signal intensity in a subregion of the anterior cingulate cortex and an increase in the dorsolateral prefrontal cortex compared to control subjects in a recent functional magnetic resonance imaging study. Patients with bipolar illness have different levels of cingulate activation, which may be due to an anomaly in the anterior cingulate or an improper modulation of the cingulate by other interacting brain regions. The frontal network, which supports inhibitory activities, may be fundamentally disrupted in bipolar illness patients [81]. Given that bipolar patients have trouble focusing and remaining on task, this functional change would be congruent with clinical observations in the condition [16,82]. According to the current research, bipolar patients who exhibit the highest inhibitory control are also likely to experience quicker returns to baseline functioning.

The mean score on most domains of PGI-memory scale including remote and recent memory, mental balance, attention and concentration, delayed recall, immediate recall, retention of similar and dissimilar pairs among cases was lower than that of controls. The results of recent memory, delayed recall and retention of similar pairs had significant difference among cases and controls. (p= 0.040, 0.002, 0.003, respectively). Similar results were obtained in a study by **Pavuluri et al** [83] with the immediate and delayed recall score in cases being 9.47 ± 2.36 and 10.00 ± 3.03 respectively which was higher when compared to the controls with a score of 12.25 ± 1.40 and 12.44 ± 1.53 respectively.

The mean retention for similar pairs memory score among cases was 5.00 ± 0.00 and among controls it was 5.00 ± 0.00. The mean retention for dissimilar pairs memory score among cases and controls was 7.73 ± 2.01 and 8.66 ± 1.30 respectively. The mean visual retention score in cases and controls was 8.93 ± 1.86 and 8.24 ± 1.45 respectively. The mean recognition score in cases and controls was 9.16 ± 0.44 and 9.24 ± 0.56 respectively. The mean total memory score in cases and controls was 82.92 ± 5.39 and 85.42 ± 4.60 respectively which fell under the category of Average/Moderate memory. The total memory score was significantly worse in cases as compared to controls.

In contrast to controls, bipolar disorder patients in the current study demonstrated deficiencies in a wide variety of cognitive abilities, including executive function, memory, processing speed and attention. This conclusion may have been influenced by the lower educational attainment of bipolar patients. Majority of the patients of bipolar disorder (34%) and healthy controls (34%) were studied up higher secondary. Similarly in a study by **Verma et al**[53], it was seen that 36.67% cases and 23.33% controls had education upto the primary level.

Generally, impaired executive functions have been described in older euthymic patients (39 to 52 years old), in those with a longer duration of illness (13 to 24 years) and more recurrent mood episodes (11 to 24) than our sample.[4] Our sample consisted of younger bipolar patients (mean age, 40.52 years) having a short duration of illness (mean, 7.82 years) and fewer episodes (mean, 3.7) than previous samples. Therefore, as a group our bipolar patients may be considered free of the deteriorative effects of long-standing illness. Recent studies have suggested that attentional performance may a viable putative endophenotype or trait characteristic for bipolar disorder. Burdick et al [84] have studied the longitudinal stability of cognitive performance in bipolar versus schizophrenia probands. They have found that many cognitive domains constantly impaired in schizophrenia and bipolar

patients showed constant attentional deficit whereas improvement on executive and memory function improved over time.

We found that increase in total number of episodes was significantly associated with low scores on Digit Forward, Digit Backward, Digit Symbol Substitution Score, Stroop Colour Test Score-Interference Score and level of memory ($p<.01$). Longer duration of illness was associated with poor psychosocial outcome as evidenced by high total score on Indian Disability Evaluation and Assessment Scale (shown in Table 29) ($p=0.00$)

We found that the lifetime total episode number and longer duration of illness significantly correlated with impaired performance on memory, executive functions and processing speed. Most of previous studies have reported that patients with a greater number of episodes and longer duration of illness suffer greater cognitive decline. Such associations have generally been thought of as indicating a progressive disease process. Our results have also confirmed these associations for a relatively young and less chronically ill patient sample.

In the current study, majority of the patients were on Divalproex (66%) followed by Lithium carbonate (26%), Olanzapine (3%), Risperidone (3%) and Oxcarbamazepine (2%). The mean TMT-A score among lithium carbonate, divalproex and others was 35.7 ± 11.79, 32.9 ± 8.97 and 42.8 ± 9.05 respectively. The mean TMT-B score among lithium carbonate, divalproex and others was 79.7 ± 26.61, 77.7 ± 24.49 and 71.8 ± 14.79 respectively.

The mean digit forward score among lithium carbonate, Divalproex and others was 4.27 ± 0.87, 4.97 ± 1.29 and 4.00 ± 1.06 respectively. The mean digit backward score among lithium carbonate, Divalproex and others was 3.58 ± 0.75, 4.06 ± 0.98 and 3.50 ± 0.75 respectively. The mean DSST Score among lithium carbonate, Divalproex and others was 44.8 ± 10.09, 56.8 ± 14.77 and 47.1 ±9.50 respectively. The Mean Interference Score among lithium carbonate, Divalproex and others

was 14.8 ± 8.76, 10.8 ± 7.79 and 12.6 ± 6.19 respectively. It showed that lithium carbonate treated bipolar patients showed deficit in cognitive performance with respect to attention, processing speed and executive functions as shown by the above mentioned tests as compared to divalproex and other mood stabilisers used. In a study by E.Mora et al,[85] executive functioning, inhibition, processing speed and verbal memory were impaired in lithium treated euthymic bipolar out-patients. Loo et al. (1981)[86] investigated the cognitive functioning of 21 non-hospitalized BMD patients treated with Lithium. A control group of 21 participants matched for age, sex, and educational level was compared with the BMD group in which the Lithium patients performed significantly poorer than the control group on the processing speed and verbal memory. Literature suggests that patients on Lithium carbonate often complain of dysphoria, lack of spontaneity, slow reaction times, intellectual inefficiency, and impairment of memory. These complaints are a common cause of poor adherence. In assessing such complaints, psychiatrists should also assess for other contributors to cognitive impairment including depression, lithium-induced hypothyroidism or hypercalcemia, other illnesses, and other drugs. As per literature, neuroprotective effects of lithium have been reported but in these reports, the duration of lifetime exposure to lithium was not known. In the prospective studies lithium was used short term (several weeks). Unlike these studies, impairment in cognitive function due to long-term use of lithium has been found. In a study done by Alper Evrensel et al.[87], it showed Bilateral temporoparietal cortical atrophy and lateral ventricular asymmetry on MRI in patient on Lithium carbonate. It is not known how chronic use of lithium makes changes in the brain and the hippocampus volume. Lithium has toxic effects on the thyroid gland and the kidney. Although it achieves a neuroprotective effect in a short time, it might also have a neurotoxic effect in the long run. In this case, cortical atrophy and cognitive dysfunction are thought to be due to long-term lithium use. In patients who use longterm lithium not only should their thyroid and the kidney

functions be monitored but their cognitive functions and changes in their brain volume should also be checked.

Better performance seen in other mood stabilisers with respect to executive functions and memory is explained multiple neurotransmitter systems involved in cognitive efficacy. Many studies on the cognitive effects of olanzapine have focused on reduced dopaminergic activity, along with more pronounced serotonergic, adrenergic or histaminic effects. For risperidone, the cognition-enhancing effect may be correlated with the combination of low-affinity antagonism of D1 and high-affinity antagonism of 5-HT2A/2C.[88]

Memory enhancement is seen in bipolar patients after prolonged lithium treatment, along with increased hippocampal volume. (Yucel et al. 2007)[89]Evidence of changes (enhancement in synaptic plasticity) in the hippocampus after lithium treatment is supplied by the animal literature as well. Enhanced long-term potentiation (LTP) has been documented after sub-chronic lithium treatment (increases in excitatory postsynaptic responses, synaptic strength, and cell firing of hippocampal granule cells in the rat dentate gyrus) (Son et al. 2003)[90]. Given that LTP is thought to be a neurophysiological basis for the development of learning and memory, these data are congruent with the functional memory enhancement seen in some of the animal studies.

There is little information available regarding the neurocognitive effects of carbamazepine and valproic acid in bipolar disorder although research in both epileptic patients and healthy volunteers have demonstrated that anticonvulsants typically cause psychomotor slowness as well as memory and attentional impairment. [91,92] . In our study, the group including Oxcarbamazepine and Atypical antipsychotics showed deficits in the domain of attention and memory as shown by poor performance on Digit span and PGI-memory scale when compared with Lithium carbonate and Divalproex treated patients but the results were insignificant. It is in concurrence with a trial with 119 euthymic BD patients, those on risperidone and

olanzapine performed worse than healthy controls on tasks requiring memory (such as the CVLT), attention (such as the TMT Part A), and verbal fluency.

The age of the patient of bipolar disorder was negatively associated with TMT-A, Digit Forward, Digit Backward and DSST whereas it was positively associated with TMT-B, Interference score of SCWT, level of memory and Global score of IDEAS. It suggests that with increasing age of the patient, there was worse performance on all tests except TMT-A and PGI memory scale. However, none of the results were statistically significant. Chronicity may be one of the reasons, so in samples with less chronic patients less verbal memory impairment could be expected. Attentional dysfunctions are less clear in our asymptomatic patients, probably due to the lack of a wide attention assessment.

However, some limitations of the study could affect the results. Medication effects are a methodological dilemma for euthymic patients, given that the majority of patients are medicated with various mood stabilizers, antidepressants, and antipsychotics, alone or in combination. It is clearly difficult and perhaps unethical to investigate drug-naive/medication-free patients and for this reason there are few and limited data on drug-free patients.

The cyclical nature of BD makes it difficult to evaluate cognitive abnormalities in this illness. Even while there are a lot of studies that use cognitive/neuropsychological performance as a secondary outcome in clinical trials evaluating the treatment of bipolar disorder, there aren't many that particularly address the management of cognitive impairment in bipolar patients. Finally, more research is required to determine the effectiveness of strategies that combine cognitive rehabilitation with biological therapies.

SUMMARY AND CONCLUSION

The present study was conducted to study the cognitive functions and functional outcome in patients of bipolar disorder in remission. In our study we noted the following points:-

- The present study showed cognitive impairment in attention, working and verbal memory along with processing speed and executive functions in a group of bipolar euthymic patients.
- After controlling for age, education and occupation, remitted bipolar patients showed significant deficits in several measures of cognition when compared to healthy controls.
- There was no significant difference between two groups in terms of distribution of age, education, occupation and marital status.
- 10% patients of bipolar disorder had family history of bipolar disorder.
- The predominant polarity of bipolar disorder was found to be depressive in 65% followed by manic in 26 % and indeterminate in 9% cases.
- The mean age of patients of bipolar disorder was 40.52 years (SD=12.34)
- The mean duration of illness in years in cases was 7.82 years (SD=6.84)
- Mean no. of hospitalisations was 0.70 (SD=0.86)
- Mean total number of episodes during the entire duration of illness was 3.7(SD=2.04)
- Mean Global score on IDEAS is 6.79 ± 2.27 which fell within Mild to moderate disability.
- We found that the lifetime total episode number and longer duration of illness significantly correlated with impaired performance on memory, executive functions and processing speed.
- We found that longer duration of illness was associated with poor psychosocial outcome as evidenced by high total score on Indian Disability Evaluation and Assessment Scale.

- In the current study, majority of the patients were on Divalproex (66%) followed by Lithium carbonate (26%), Olanzapine (3%), Risperidone (3%) and Oxcarbamazepine (2%).
- The study showed that lithium carbonate treated bipolar patients showed significant deficits in cognitive performance with respect to attention, processing speed and executive functions as compared to divalproex and other mood stabilisers used as shown by the neuro-psychological tests.
- The group including Oxcarbamazepine and Atypical antipsychotics showed deficits in the domain of attention and memory as shown by poor performance on Digit span and PGI-memory scale when compared with Lithium carbonate and Divalproex treated patients.
- Our study demonstrates that specific cognitive deficits exist in patients in the euthymic phase of bipolar disorder. These deficits can cause significant impairment in daily life of individuals with BPAD. Therefore, there is a need to develop rehabilitative and treatment models aimed at addressing/improving these cognitive deficits to achieve better functioning on recovery.

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SR. NO	PATIENT NAME	MRD	GROUP	AGE	AGE GROUP	SEX	MARITAL STATUS	EDUCATION	OCCUPATION	EDUCATION GP	OCCUPATION GP	FAMILY TYPE	RELIGION	DURATION OF ILLNESS(IN YEARS)	FAMILY HISTORY OF PSYCHIATRIC ILLNESS	PREDOMINANT POLARITY	NO. OF MANIC EPISODES
1	GK	1274336	CASES	38	2	M	MARRIED	HIGHER SECONDARY	PROFESSIONAL	2	4	NUCLEAR	HINDU	12	0	MANIA	2
2	JS	1326778	CASES	23	1	M	UNMARRIED	GRADUATE	UNEMPLOYED	4	8	NUCLEAR	SIKH	3	0	MANIA	3
3	IS	1360580	CASES	27	1	M	MARRIED	GRADUATE	SKILLED WORKER	4	7	NUCLEAR	SIKH	2	0	MANIA	2
4	JS	603245	CASES	43	3	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	JOINT	HINDU	4	PATERNAL UNCLE OF FATHER	NONE	2
5	Y	1361596	CASES	23	1	M	UNMARRIED	GRADUATE	UNEMPLOYED	4	8	NUCLEAR	HINDU	2	MOTHER	NONE	1
6	NKG	1353755	CASES	31	2	M	UNMARRIED	GRADUATE	BUSINESSMAN	4	1	NUCLEAR	HINDU	2	0	NONE	1
7	LS	741442	CASES	48	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	NUCLEAR	SIKH	19	0	MANIA	8
8	NK	1372786	CASES	40	2	M	MARRIED	HIGHER SECONDARY	BUSINESSMAN	2	1	NUCLEAR	HINDU	4	0	MANIA	2
9	AS	1385395	CASES	47	3	M	MARRIED	POST-GRADUATE	PROFESSIONAL	5	4	NUCLEAR	SIKH	2	0	MANIA	2
10	SB	1130570	CASES	25	1	M	UNMARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	HINDU	5	0	MANIA	3
11	AVG	1333058	CASES	39	2	M	MARRIED	GRADUATE	BUSINESSMAN	4	1	EXTENDED NUCLEAR	HINDU	2	MOTHER	DEPRESSIVE	1
12	AR	707509	CASES	45	3	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	EXTENDED NUCLEAR	HINDU	25	0	MANIA	6
13	SS	1196304	CASES	30	1	M	MARRIED	POST-GRADUATE	PROFESSIONAL	5	4	NUCLEAR	SIKH	2	0	NONE	1
14	SS	1281634	CASES	48	3	M	MARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	NUCLEAR	HINDU	5	0	DEPRESSIVE	1
15	JK	1285863	CASES	53	4	F	MARRIED	GRADUATE	UNEMPLOYED	4	3	EXTENDED NUCLEAR	SIKH	20	0	DEPRESSIVE	1
16	SR	1287042	CASES	34	2	F	UNMARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	HINDU	5	0	MANIA	2
17	RD	464428	CASES	32	2	F	MARRIED	MATRICULATION	UNEMPLOYED	3	8	NUCLEAR	HINDU	2	0	MANIA	1
18	PK	1287183	CASES	26	1	M	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	2	8	NUCLEAR	SIKH	2	0	DEPRESSIVE	1
19	BK	56207	CASES	51	4	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	EXTENDED NUCLEAR	SIKH	30	0	MANIA	3
20	DK	1281719	CASES	61	5	F	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	EXTENDED NUCLEAR	SIKH	6	0	DEPRESSIVE	1
21	NS	1293233	CASES	28	1	M	MARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	SIKH	2	0	MANIA	1
22	MK	1284752	CASES	25	1	M	UNMARRIED	MATRICULATION	SKILLED WORKER	3	2	JOINT	HINDU	2	0	MANIA	1
23	CK	1288935	CASES	66	5	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	JOINT	SIKH	20	0	DEPRESSIVE	1
24	CS	1121651	CASES	52	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	NUCLEAR	HINDU	10	0	MANIA	3
25	HS	687902	CASES	26	1	M	UNMARRIED	MATRICULATION	UNEMPLOYED	3	3	JOINT	HINDU	2	0	MANIA	1
26	NK	72544	CASES	49	3	M	MARRIED	MATRICULATION	UNEMPLOYED	3	3	JOINT	SIKH	5	0	DEPRESSIVE	0
27	VK	1386507	CASES	62	5	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	HINDU	2	0	MANIA	2
28	KS	1383390	CASES	45	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	SIKH	12	0	MANIA	2
29	AK	1385170	CASES	32	2	M	UNMARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	NUCLEAR	HINDU	2	0	DEPRESSIVE	2
30	GS	1369653	CASES	32	2	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	JOINT	SIKH	8	0	DEPRESSIVE	1
31	SS	1354567	CASES	42	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	EXTENDED NUCLEAR	HINDU	22	0	MANIA	6
32	KS	632899	CASES	39	2	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	SIKH	2	0	MANIA	2
33	AM	726974	CASES	29	1	M	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	2	8	NUCLEAR	HINDU	13	0	MANIA	6
34	RS	1376302	CASES	62	5	M	MARRIED	MATRICULATION	SKILLED WORKER	3	2	EXTENDED NUCLEAR	SIKH	2	FATHER	MANIA	2
35	RB	1383638	CASES	46	3	M	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	JOINT	HINDU	2	0	DEPRESSIVE	1
36	BS	337900	CASES	48	3	M	MARRIED	MATRICULATION	SKILLED WORKER	3	2	JOINT	SIKH	10	0	DEPRESSIVE	0
37	SS	762353	CASES	36	2	M	MARRIED	HIGHER SECONDARY	BUSINESSMAN	2	1	JOINT	SIKH	10	0	MANIA	2
38	PS	1345318	CASES	25	1	M	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	8	JOINT	SIKH	4	0	MANIA	4
39	DG	1347281	CASES	20	1	F	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	2	8	JOINT	HINDU	4	0	DEPRESSIVE	1
40	MD	1350576	CASES	55	4	F	MARRIED	ILLITERATE	UNEMPLOYED	1	3	JOINT	HINDU	5	0	DEPRESSIVE	0
41	AK	1321096	CASES	45	3	F	MARRIED	POST-GRADUATE	UNEMPLOYED	5	3	EXTENDED NUCLEAR	SIKH	4	MOTHER	DEPRESSIVE	1
42	AS	929381	CASES	63	5	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	EXTENDED NUCLEAR	SIKH	9	0	MANIA	2
43	KK	1362077	CASES	63	5	F	MARRIED	ILLITERATE	UNEMPLOYED	1	3	JOINT	SIKH	2	0	MANIA	2
44	GS	831727	CASES	56	4	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	JOINT	SIKH	18	0	NONE	3
45	IS	1141787	CASES	22	1	M	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	2	8	JOINT	SIKH	2	GRANDFATHER	MANIA	2
46	MS	1151573	CASES	29	1	M	UNMARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	JOINT	SIKH	10	0	MANIA	3
47	DS	1158913	CASES	38	2	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	JOINT	SIKH	9	0	MANIA	2
48	SN	321418	CASES	51	4	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	HINDU	6	BROTHER	MANIA	8
49	AA	1229625	CASES	48	3	M	MARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	HINDU	26	0	DEPRESSIVE	1
50	BJ	1124229	CASES	32	2	F	MARRIED	POST-GRADUATE	UNEMPLOYED	5	3	JOINT	HINDU	4	0	MANIA	2
51	RS	1144256	CASES	25	1	M	UNMARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	JOINT	SIKH	7	0	MANIA	3
52	RS	1234592	CASES	32	2	M	MARRIED	ILLITERATE	UNEMPLOYED	1	8	JOINT	SIKH	10	0	MANIA	3
53	AS	1254006	CASES	28	1	M	UNMARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	JOINT	SIKH	5	0	DEPRESSIVE	1

SR. NO	PATIENT NAME	NO. OF DEPRESSIVE EPISODES	Total episodes	NO. OF HOSPITALISATIONS	MOOD STABILISERS	TRAIL MAKING TEST SCORE- A	TRAIL MAKING TEST SCORE- B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	STROOP COLOUR TEST SCORE-COLOUR SCORE	WORD SCORE	COLOUR-WORD SCORE	PREDICTED COLOUR WORD	INTERFERENCE SCORE	REMOTE MEMORY	RECENT MEMORY	MENTAL BALANCE	ATTENTION & CONCENTRATION	DELAYED RECALL
1	GK	0	2	1	VALPROATE	36.2	63	4	4	45	40	55	41	23.15789474	17.84210526	4	5	9	23	10
2	JS	0	3	2	VALPROATE	59	153	6	4	31	90	65	38	37.74193548	0.258064516	5	5	9	19	10
3	IS	1	3	1	VALPROATE	24.8	48	5	4	66	45	87	55	29.65909091	25.34090909	5	5	9	20	10
4	JS	2	4	2	VALPROATE	40	52	3	3	52	86	66	40	37.34210526	2.657894737	5	5	9	15	10
5	Y	1	2	1	LITHIUM	41.9	66	4	3	46	84	68	52	37.57894737	14.42105263	5	5	9	15	10
6	NKG	1	2	1	VALPROATE	42.3	55	5	3	33	52	69	55	29.65289256	25.34710744	6	5	9	17	10
7	LS	1	9	3	VALPROATE	36.2	63	4	4	39	64	75	40	34.5323741	5.467625899	5	4	7	18	10
8	NK	0	2	1	VALPROATE	37.5	48	4	4	40	71	79	39	37.39333333	1.606666667	4	5	9	19	10
9	AS	1	3	1	VALPROATE	31.5	56	6	5	70	73	74	40	36.74829932	3.25170068	8	5	9	15	10
10	SB	0	3	2	VALPROATE	44.6	89	5	4	66	61	78	52	34.23021583	17.76978417	8	5	9	18	10
11	AVG	3	4	2	LITHIUM	55.3	88	5	4	67	43	85	53	28.5546875	24.4453125	8	5	9	17	10
12	AR	1	7	2	LITHIUM	45	55	4	3	52	52	65	54	28.88888889	25.11111111	3	3	9	19	10
13	SS	1	2	0	LITHIUM	52	63	5	3	45	59	88	51	35.31972789	15.68027211	8	5	9	15	10
14	SS	2	3	0	LITHIUM	25.1	48	6	5	43	51	87	56	32.15217391	23.84782609	4	5	9	15	10
15	JK	5	6	0	VALPROATE	26	59	4	4	46	54	75	42	31.39534884	10.60465116	4	5	9	17	10
16	SR	1	3	0	VALPROATE	28	52	3	2	48	56	72	37	31.5	5.5	8	5	9	15	10
17	RD	0	1	0	RISPERIDONE	26	81	3	3	49	57	70	38	30.93023256	7.069767442	4	3	9	24	10
18	PK	1	2	0	LITHIUM	36.2	70	4	4	50	85	71	42	38.68589744	3.314102564	6	4	4	15	10
19	BK	2	5	0	OLANZAPINE	38.2	64	5	5	36	74	65	53	34.60431655	18.39568345	8	5	9	23	10
20	DK	3	4	0	VALPROATE	41	63	5	4	38	76	64	55	34.74285714	20.25714286	8	5	9	22	10
21	NS	0	1	1	VALPROATE	28.9	94	4	4	37	63	65	42	31.9921875	10.0078125	6	5	9	16	10
22	MK	0	1	1	VALPROATE	36.4	98	3	4	55	50	63	39	27.87610619	11.12389381	6	5	9	15	10
23	CK	4	5	2	LITHIUM	25.3	55	5	3	62	66	62	40	31.96875	8.03125	6	4	5	19	10
24	CS	1	4	1	VALPROATE	24.9	75	4	4	34	77	61	56	34.03623188	21.96376812	5	5	6	18	10
25	HS	0	1	0	LITHIUM	35.4	71	3	4	39	36	75	54	24.32432432	29.67567568	6	4	9	20	10
26	NK	2	2	0	LITHIUM	40	85	4	3	30	60	74	36	33.13432836	2.865671642	6	5	9	21	10
27	VK	0	2	2	VALPROATE	25	64	5	3	48	54	76	39	31.56923077	7.430769231	5	5	8	15	10
28	KS	1	3	0	VALPROATE	26	54	5	5	49	67	71	42	34.47101449	7.528985507	5	5	6	15	10
29	AK	2	4	1	LITHIUM	27	52	4	4	37	48	65	46	27.61061947	18.38938053	4	5	6	14	10
30	GS	2	3	0	VALPROATE	23.6	53	3	2	30	55	84	53	33.23741007	19.76258993	4	5	6	16	10
31	SS	4	10	2	VALPROATE	25.3	58	5	3	45	95	80	51	43.42857143	7.571428571	6	4	9	9	10
32	KS	0	2	1	VALPROATE	30.2	59	4	4	40	53	82	53	32.19259259	20.80740741	8	5	9	9	10
33	AM	0	6	2	VALPROATE	24.1	58	5	5	56	74	80	38	38.44155844	-0.441558442	6	1	9	5	10
34	RS	0	2	0	VALPROATE	36	78	4	4	53	80	86	39	41.44578313	-2.445783133	7	5	9	15	10
35	RB	2	3	0	LITHIUM	24	76	5	5	51	64	84	40	36.32432432	3.675675676	6	5	6	19	10
36	BS	3	3	0	OXCARBAMAZEPINE	45.6	72	3	4	59	88	85	45	43.23699422	1.76300578	4	4	6	19	10
37	SS	1	3	0	VALPROATE	46.3	73	4	3	35	75	67	43	35.38732394	7.612676056	6	5	9	15	10
38	PS	0	4	0	VALPROATE	25.3	84	5	3	62	74	69	53	35.70629371	17.29370629	3	5	6	15	10
39	DG	2	3	0	VALPROATE	41.3	77	5	4	48	72	62	38	33.31343284	4.686567164	6	5	9	9	10
40	MD	2	2	0	LITHIUM	53.2	95	3	3	50	64	56	40	29.86666667	10.13333333	5	5	6	12	7
41	AK	3	4	0	LITHIUM	26	90	6	4	33	68	58	52	31.3015873	20.6984127	4	5	7	13	10
42	AS	1	3	0	VALPROATE	38.9	77	5	3	37	60	60	55	30	25	6	5	5	15	10
43	KK	0	2	0	VALPROATE	34.8	111	3	3	49	75	85	54	39.84375	14.15625	4	5	6	16	10
44	GS	3	6	1	VALPROATE	30	106	4	3	42	70	84	43	38.18181818	4.818181818	6	5	5	16	10
45	IS	0	2	1	VALPROATE	25	134	4	3	45	77	65	49	35.24647887	13.75352113	6	5	6	16	10
46	MS	0	3	1	VALPROATE	24	115	5	3	53	95	68	57	39.63190184	17.36809816	5	5	4	16	10
47	DS	1	3	1	VALPROATE	36	86	5	4	48	44	74	47	27.59322034	19.40677966	6	5	5	11	10
48	SN	1	9	3	VALPROATE	29	92	4	4	65	53	79	56	31.71969697	24.28030303	6	5	6	17	10
49	AA	4	5	2	LITHIUM	36	84	4	3	39	55	80	50	32.59259259	17.40740741	6	5	6	12	10
50	BJ	0	2	0	VALPROATE	49.8	55	5	5	46	51	84	40	31.73333333	8.266666667	6	5	6	11	10
51	RS	1	4	0	VALPROATE	25.6	64.5	5	3	53	57	76	39	32.57142857	6.428571429	4	4	7	16	6
52	RS	2	5	1	RISPERIDONE	38.9	62.5	3	3	41	59	71	42	32.22307692	9.776923077	5	5	6	12	7
53	AS	2	3	2	OLANZAPINE	45.2	56	4	3	55	54	65	46	29.49579832	16.50420168	5	5	6	13	7

SR. NO	PATIENT NAME	IMMEDIATE RECALL	RETENTION FOR SIMILAR PAIRS	RETENTION FOR DISSIMILAR PAIRS	VISUAL RETENTION	RECOGNITION	LEVELS OF MEMORY	IDEAS- Self-care	Interpersonal activities	Communication and understanding	Work	Total score (A)	Duration of illness score (B)	Global score (A+B)
1	GK	10	5	8	8	9	91	1	0	0	2	3	4	7
2	JS	11	5	8	8	9	89	2	1	0	1	4	2	6
3	IS	11	5	8	8	9	90	0	1	2	2	5	1	6
4	JS	11	5	8	9	9	86	1	0	1	2	4	2	6
5	Y	12	5	7	8	10	86	0	1	0	1	2	1	3
6	NKG	12	5	8	7	9	88	0	2	0	2	4	1	5
7	LS	12	5	9	7	10	87	3	1	0	3	7	4	11
8	NK	11	5	8	8	10	89	0	0	2	1	3	2	5
9	AS	11	5	5	7	10	85	0	1	1	1	3	1	4
10	SB	11	5	8	7	9	90	2	0	2	2	6	2	8
11	AVG	11	5	9	7	9	90	0	1	1	1	3	1	4
12	AR	12	5	8	8	10	87	2	3	1	4	10	4	14
13	SS	11	5	3	8	10	84	1	1	2	1	5	1	6
14	SS	12	5	9	8	9	86	0	1	0	1	2	2	4
15	JK	11	5	6	9	9	85	0	2	1	1	4	4	8
16	SR	12	5	8	8	10	90	1	2	1	2	6	2	8
17	RD	10	5	5	9	9	88	0	1	0	2	3	1	4
18	PK	11	5	15	8	8	86	0	2	2	3	7	1	8
19	BK	10	5	9	6	10	95	2	2	1	1	6	4	10
20	DK	11	5	8	12	9	99	0	0	0	2	2	3	5
21	NS	12	5	7	5	9	84	1	2	1	2	6	1	7
22	MK	11	5	9	6	9	85	0	2	0	1	2	1	3
23	CK	10	5	5	8	8	80	0	1	2	1	4	4	8
24	CS	11	5	7	12	10	89	3	2	2	1	8	4	12
25	HS	12	5	6	9	10	91	1	0	1	1	3	1	4
26	NK	11	5	9	9	9	94	0	1	0	1	2	2	4
27	VK	12	5	11	9	9	89	1	2	1	1	5	1	6
28	KS	9	5	5	12	10	82	1	0	1	1	3	4	7
29	AK	11	5	9	8	9	81	2	1	1	2	6	1	7
30	GS	12	5	8	9	9	84	1	1	2	0	4	3	7
31	SS	10	5	9	12	10	84	3	1	0	1	5	4	9
32	KS	12	5	6	12	9	85	0	1	1	2	4	1	5
33	AM	12	5	4	13	9	74	2	3	2	1	8	4	12
34	RS	10	5	3	13	9	86	0	2	1	2	5	1	6
35	RB	9	5	6	7	9	82	0	1	1	1	3	1	4
36	BS	12	5	7	7	9	83	0	1	1	2	4	4	8
37	SS	12	5	9	6	9	86	1	1	0	3	5	4	9
38	PS	12	5	8	8	9	81	2	1	1	3	7	2	9
39	DG	12	5	5	14	10	85	1	0	1	1	3	2	5
40	MD	9	5	8	9	9	75	0	1	0	2	3	2	5
41	AK	12	5	7	7	9	79	0	0	2	3	5	2	6
42	AS	12	5	6	12	10	86	0	1	1	1	3	3	6
43	KK	12	5	5	9	10	82	1	0	0	2	3	1	4
44	GS	12	5	9	7	9	84	1	1	1	2	5	4	9
45	IS	9	5	9	7	9	82	2	2	0	0	4	1	5
46	MS	9	5	9	12	10	85	1	2	2	1	4	4	8
47	DS	12	5	9	9	9	81	1	2	2	2	7	3	10
48	SN	8	5	9	7	9	82	2	3	1	1	7	3	10
49	AA	12	5	9	7	9	81	1	2	0	0	3	4	7
50	BJ	12	5	8	9	9	81	2	1	1	1	5	3	8
51	RS	12	5	8	9	9	80	0	0	1	2	3	3	6
52	RS	9	5	8	9	9	75	0	1	1	3	5	4	9
53	AS	12	5	8	7	9	77	2	2	2	1	7	2	9

SR. NO	PATIENT NAME	MRD	GROUP	AGE	AGE GROUP	SEX	MARITAL STATUS	EDUCATION	OCCUPATION	EDUCATION GP	OCCUPATION GP	FAMILY TYPE	RELIGION	DURATION OF ILLNESS(IN YEARS)	FAMILY HISTORY OF PSYCHIATRIC ILLNESS	PREDOMINANT POLARITY	NO. OF MANIC EPISODES
54	SY	334966	CASES	27	1	M	UNMARRIED	GRADUATE	UNEMPLOYED	4	8	JOINT	HINDU	4	0	DEPRESSIVE	1
55	SS	594521	CASES	37	2	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	SIKH	2	0	MANIA	1
56	HS	1017990	CASES	18	1	M	UNMARRIED	MATRICULATION	UNEMPLOYED	3	8	JOINT	SIKH	6	GRANDFATHER	MANIA	3
57	SS	732070	CASES	27	1	M	MARRIED	MATRICULATION	SKILLED WORKER	3	2	NUCLEAR	SIKH	5	0	DEPRESSIVE	1
58	KS	68342	CASES	48	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	JOINT	SIKH	14	0	MANIA	3
59	KS	1281593	CASES	59	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	JOINT	SIKH	11	0	MANIA	2
60	GS	740023	CASES	32	2	M	UNMARRIED	MATRICULATION	SKILLED WORKER	3	7	NUCLEAR	SIKH	3	0	MANIA	2
61	BR	68231	CASES	27	1	M	MARRIED	ILLITERATE	UNEMPLOYED	1	3	JOINT	HINDU	2	0	MANIA	2
62	PT	1161888	CASES	30	1	M	UNMARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	HINDU	4	0	MANIA	2
63	BS	1313721	CASES	40	2	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	NUCLEAR	SIKH	7	0	MANIA	2
64	AK	1390693	CASES	41	3	M	MARRIED	GRADUATE	BUSINESSMAN	4	1	NUCLEAR	HINDU	9	0	MANIA	3
65	PR	774917	CASES	62	5	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	EXTENDED NUCLEAR	HINDU	22	0	MANIA	2
66	AK	904772	CASES	29	1	M	UNMARRIED	ILLITERATE	SKILLED WORKER	1	7	JOINT	HINDU	10	0	MANIA	2
67	RK	986036	CASES	41	3	M	MARRIED	ILLITERATE	SKILLED WORKER	1	7	EXTENDED NUCLEAR	HINDU	10	0	DEPRESSIVE	0
68	JK	112456	CASES	42	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	HINDU	8	0	MANIA	5
69	JS	1396547	CASES	29	1	M	UNMARRIED	GRADUATE	UNEMPLOYED	4	8	NUCLEAR	SIKH	4	0	MANIA	2
70	CA	1084041	CASES	42	3	M	MARRIED	GRADUATE	BUSINESSMAN	4	1	JOINT	HINDU	3	0	DEPRESSIVE	1
71	BS	1415477	CASES	42	3	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	JOINT	SIKH	3	0	MANIA	2
72	HS	1395238	CASES	29	1	M	UNMARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	NUCLEAR	SIKH	3	0	MANIA	2
73	HS	1392853	CASES	60	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	NUCLEAR	SIKH	4	0	MANIA	2
74	BS	1378290	CASES	37	2	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	JOINT	SIKH	2	0	MANIA	2
75	YSB	1392170	CASES	28	1	M	UNMARRIED	GRADUATE	BUSINESSMAN	4	1	JOINT	SIKH	2	0	MANIA	2
76	NR	570233	CASES	30	1	F	MARRIED	POST-GRADUATE	UNEMPLOYED	5	3	NUCLEAR	HINDU	3	0	MANIA	3
77	GS	1423249	CASES	35	2	M	MARRIED	MATRICULATION	UNEMPLOYED	3	8	NUCLEAR	SIKH	2	0	MANIA	2
78	N	84843	CASES	34	2	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	JOINT	HINDU	3	0	MANIA	1
79	GS	171303	CASES	42	3	M	MARRIED	POST-GRADUATE	UNEMPLOYED	5	8	EXTENDED NUCLEAR	HINDU	9	0	MANIA	2
80	AK	920951	CASES	54	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	NUCLEAR	HINDU	13	0	NONE	0
81	AB	70438	CASES	44	3	F	UNMARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	HINDU	15	0	DEPRESSIVE	1
82	PK	48378	CASES	36	2	F	MARRIED	ILLITERATE	UNEMPLOYED	1	3	JOINT	HINDU	4	0	NONE	0
83	HS	1429844	CASES	43	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	NUCLEAR	SIKH	8	0	DEPRESSIVE	4
84	VK	1011583	CASES	24	1	M	UNMARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	NUCLEAR	HINDU	2	0	MANIA	3
85	SG	1435219	CASES	50	3	M	MARRIED	GRADUATE	BUSINESSMAN	4	1	NUCLEAR	HINDU	3	0	EQUAL	2
86	MS	1430680	CASES	43	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	EXTENDED NUCLEAR	SIKH	15	0	MANIA	5
87	Y	909433	CASES	28	1	F	MARRIED	GRADUATE	PROFESSIONAL	4	4	EXTENDED NUCLEAR	HINDU	9	0	MANIA	5
88	NS	1435094	CASES	35	2	M	MARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	NUCLEAR	SIKH	2	0	MANIA	1
89	CS	29903	CASES	61	5	M	MARRIED	GRADUATE	SKILLED WORKER	4	7	NUCLEAR	SIKH	6	0	MANIA	2
90	MK	1434266	CASES	47	3	F	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	NUCLEAR	SIKH	22	0	MANIA	4
91	AS	101214	CASES	41	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	SIKH	11	0	MANIA	3
92	MK	1434985	CASES	32	2	M	MARRIED	GRADUATE	SKILLED WORKER	4	7	NUCLEAR	HINDU	9	PATERNAL COUSIN	DEPRESSIVE	1
93	RS	1033395	CASES	53	4	M	MARRIED	GRADUATE	RETIRED	4	5	JOINT	SIKH	30	MOTHER/SIBLINGS	MANIA	5
94	LS	1437878	CASES	35	2	M	MARRIED	ILLITERATE	SKILLED WORKER	1	7	JOINT	SIKH	16	0	DEPRESSIVE	0
95	CK	1438049	CASES	57	4	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	JOINT	SIKH	10	0	EQUAL	1
96	PK	1433384	CASES	51	4	F	MARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	JOINT	SIKH	10	0	DEPRESSIVE	1
97	JS	1434845	CASES	56	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	EXTENDED NUCLEAR	SIKH	10	0	MANIA	0
98	JS	1434814	CASES	59	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	EXTENDED NUCLEAR	SIKH	3	0	MANIA	2
99	JR	1435304	CASES	55	4	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	JOINT	SIKH	2	0	DEPRESSIVE	0
100	AH	1435209	CASES	65	5	M	MARRIED	GRADUATE	PROFESSIONAL	4	4	JOINT	MUSLIM	22	0	MANIA	2
1	RK		CONTROL	26	1	F	UNMARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	SIKH	-	-	-	-
2	AK		CONTROL	46	3	F	MARRIED	MATRICULATION	UNEMPLOYED	3	8	NUCLEAR	SIKH	-	-	-	-
3	GS		CONTROL	25	1	M	MARRIED	MATRICULATION	SEMI-SKILLED	3	6	NUCLEAR	SIKH	-	-	-	-
4	NK		CONTROL	26	1	F	MARRIED	MATRICULATION	UNEMPLOYED	3	8	NUCLEAR	SIKH	-	-	-	-
5	AS		CONTROL	30	1	M	MARRIED	GRADUATE	SEMI-SKILLED	4	6	NUCLEAR	SIKH	-	-	-	-
6	GB		CONTROL	40	2	F	UNMARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	HINDU	-	-	-	-

SR. NO	PATIENT NAME	NO. OF DEPRESSIVE EPISODES	Total episodes	NO. OF HOSPITALISATIONS	MOOD STABILISERS	TRAIL MAKING TEST SCORE- A	TRAIL MAKING TEST SCORE- B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	STROOP COLOUR TEST SCORE-COLOUR SCORE	WORD SCORE	COLOUR-WORD SCORE	PREDICTED COLOUR WORD	INTERFERENCE SCORE	REMOTE MEMORY	RECENT MEMORY	MENTAL BALANCE	ATTENTION & CONCENTRATION	DELAYED RECALL
54	SY	2	3	0	RISPERIDONE	45	88	6	3	49	53	84	53	32.49635036	20.50364964	5	5	4	9	10
55	SS	0	1	0	VALPROATE	55	97	3	4	42	58	80	51	33.62318841	17.37681159	5	4	5	14	10
56	HS	1	4	0	VALPROATE	26	136	4	3	67	59	82	53	34.31205674	18.68794326	4	5	8	16	8
57	SS	2	3	0	LITHIUM	39	134	4	4	46	54	80	38	32.23880597	5.76119403	4	5	8	17	8
58	KS	1	4	1	VALPROATE	31	102	4	3	48	54	86	39	33.17142857	5.828571429	5	5	7	18	8
59	KS	1	3	0	VALPROATE	24	123	3	4	39	78	84	40	40.44444444	-0.444444444	4	4	7	9	8
60	GS	0	2	0	VALPROATE	55	150	5	3	35	63	85	45	36.18243243	8.817567568	4	5	7	13	10
61	BR	0	2	0	OLANZAPINE	58	95	4	4	33	55	67	43	30.20491803	12.79508197	4	5	7	14	7
62	PT	1	3	0	VALPROATE	44.6	89	5	4	66	43	85	53	28.5546875	24.4453125	4	5	7	11	10
63	BS	0	2	0	VALPROATE	55.3	88	5	4	67	52	65	54	28.88888889	25.11111111	4	5	8	10	10
64	AK	2	5	0	VALPROATE	45	55	4	3	52	59	88	51	35.31972789	15.68027211	5	5	4	9	10
65	PR	1	3	0	LITHIUM	52	63	5	3	45	51	87	56	32.15217391	23.84782609	5	5	6	9	5
66	AK	1	3	0	VALPROATE	25.1	48	6	5	43	54	75	42	31.39534884	10.60465116	4	5	7	15	6
67	RK	3	3	0	VALPROATE	26	59	4	4	46	56	72	37	31.5	5.5	4	5	6	9	10
68	JK	2	7	1	VALPROATE	28	52	3	2	48	57	70	38	31.41732283	6.582677165	8	5	9	9	10
69	JS	0	2	0	LITHIUM	26	81	3	3	49	85	71	42	38.68589744	3.314102564	5	4	9	12	10
70	CA	2	3	0	VALPROATE	36.2	70	4	4	50	74	65	53	34.60431655	18.39568345	4	5	7	16	6
71	BS	0	2	0	VALPROATE	38.2	64	5	5	36	76	64	55	34.74285714	20.25714286	4	5	6	17	8
72	HS	1	3	1	VALPROATE	41	63	5	4	38	63	65	42	31.9921875	10.0078125	5	5	6	14	7
73	HS	1	3	2	LITHIUM	28.9	94	4	4	37	50	63	39	27.87610619	11.12389381	4	5	5	13	7
74	BS	2	4	1	VALPROATE	36.4	98	3	4	55	66	62	40	31.96875	8.03125	5	5	6	9	10
75	YSB	0	2	1	VALPROATE	25.3	55	5	3	62	77	61	56	34.03623188	21.96376812	4	5	7	16	10
76	NR	1	4	1	LITHIUM	24.9	75	4	4	34	36	75	54	24.32432432	29.67567568	5	5	9	11	10
77	GS	0	2	1	VALPROATE	35.4	71	3	4	39	60	74	36	33.13432836	2.865671642	5	5	6	9	10
78	N	1	2	0	VALPROATE	40	85	4	3	30	54	76	39	31.56923077	7.430769231	8	5	9	11	10
79	GS	0	2	0	LITHIUM	25	64	5	3	48	67	71	42	34.47101449	7.528985507	7	3	9	5	10
80	AK	2	2	0	VALPROATE	26	54	5	5	49	48	65	46	27.61061947	18.38938053	7	5	9	6	10
81	AB	2	3	1	LITHIUM	27	52	4	4	37	55	84	53	33.23741007	19.76258993	7	5	9	9	10
82	PK	1	1	0	LITHIUM	23.6	53	3	2	30	95	80	51	43.42857143	7.571428571	7	5	5	13	7
83	HS	1	5	0	VALPROATE	25.3	58	5	3	45	53	82	53	32.19259259	20.80740741	5	5	6	9	10
84	VK	0	3	3	VALPROATE	30.2	59	4	4	40	74	80	38	38.44155844	-0.441558442	4	5	7	16	7
85	SG	3	5	1	VALPROATE	24.1	58	5	5	56	75	67	43	35.38732394	7.612676056	5	5	6	9	10
86	MS	0	5	1	VALPROATE	36	78	4	4	53	74	69	53	35.70629371	17.29370629	4	5	7	12	10
87	Y	0	5	2	LITHIUM	24	76	5	5	51	72	62	38	33.31343284	4.686567164	4	4	5	15	10
88	NS	0	1	1	VALPROATE	45.6	72	3	4	59	64	56	40	29.86666667	10.13333333	5	5	6	9	7
89	CS	1	3	1	VALPROATE	46.3	73	4	3	35	68	58	52	31.3015873	20.6984127	8	5	9	10	10
90	MK	0	4	1	VALPROATE	25.3	84	5	3	62	60	60	55	30	25	4	5	7	17	7
91	AS	2	5	2	VALPROATE	41.3	77	5	4	48	75	85	54	39.84375	14.15625	8	5	8	15	8
92	MK	5	6	1	VALPROATE	53.2	95	3	3	50	70	84	43	38.18181818	4.818181818	8	5	8	9	8
93	RS	2	7	3	OXCARBAMAZEPINE	45.2	56	4	3	55	77	65	49	35.24647887	13.75352113	5	4	9	6	10
94	LS	2	2	0	VALPROATE	45	88	6	3	49	95	68	57	39.63190184	17.36809816	8	4	7	15	10
95	CK	1	2	0	LITHIUM	55	97	3	4	42	44	74	47	27.59322034	19.40677966	8	5	9	9	10
96	PK	3	4	0	LITHIUM	26	136	4	3	67	53	79	56	31.71969697	24.28030303	7	5	9	15	8
97	JS	1	1	0	VALPROATE	39	134	4	4	46	55	80	50	32.59259259	17.40740741	8	5	9	15	10
98	JS	1	3	0	VALPROATE	31	102	4	3	48	51	84	40	31.73333333	8.266666667	4	3	6	15	10
99	JR	2	2	0	VALPROATE	24	123	3	4	39	57	76	39	32.57142857	6.428571429	8	5	9	15	10
100	AH	0	2	0	LITHIUM	55	150	5	3	35	59	71	42	32.22307692	9.776923077	6	5	8	9	9
1	RK	-	0	-	-	37	126	8	5	66	55	82	41	32.91970803	8.080291971	4	5	9	22	10
2	AK	-	0	-	-	26	111	7	4	51	65	62	38	31.73228346	6.267716535	5	5	9	19	10
3	GS	-	0	-	-	40	86	5	3	82	87	103	55	47.16315789	7.836842105	5	5	9	20	10
4	NK	-	0	-	-	23	75	6	6	52	66	90	40	38.07692308	1.923076923	5	5	9	15	10
5	AS	-	0	-	-	20	73	4	4	66	68	70	52	34.49275362	17.50724638	5	5	9	9	10
6	GB	-	0	-	-	30	56	5	5	70	69	85	55	38.08441558	16.91558442	6	5	9	19	10

SR. NO	PATIENT NAME	IMMEDIATE RECALL	RETENTION FOR SIMILAR PAIRS	RETENTION FOR DISSIMILAR PAIRS	VISUAL RETENTION	RECOGNITION	LEVELS OF MEMORY	IDEAS- Self-care	Interpersonal activities	Communication and understanding	Work	Total score (A)	Duration of illness score (B)	Global score (A+B)
54	SY	12	5	7	9	9	75	0	0	0	0	0	2	2
55	SS	9	5	8	9	9	78	2	1	1	2	6	1	7
56	HS	12	5	8	9	9	84	0	2	0	2	4	3	7
57	SS	9	5	8	9	9	82	0	0	0	3	3	2	5
58	KS	12	5	8	9	9	86	0	1	1	1	3	4	7
59	KS	12	5	8	9	9	75	1	2	2	2	7	4	11
60	GS	12	5	8	7	9	80	0	0	1	2	3	2	5
61	BR	8	5	8	9	9	76	0	1	1	1	3	1	4
62	PT	12	5	9	9	9	81	2	0	1	2	5	2	7
63	BS	12	5	9	9	9	81	0	1	0	1	2	3	5
64	AK	10	5	9	9	9	75	1	2	1	1	5	3	8
65	PR	12	5	9	9	9	74	0	1	1	1	3	4	7
66	AK	12	5	9	9	9	81	0	1	2	1	4	4	8
67	RK	12	5	5	9	9	74	3	0	1	1	5	4	9
68	JK	11	5	15	9	10	91	1	3	1	3	8	3	11
69	JS	12	5	9	7	8	81	1	0	0	1	2	2	4
70	CA	12	5	9	7	9	80	1	1	0	1	3	2	5
71	BS	10	5	9	7	9	80	1	1	2	0	4	2	6
72	HS	12	5	9	9	9	81	1	0	1	1	3	2	5
73	HS	10	5	9	9	9	76	1	0	0	2	3	2	5
74	BS	12	5	5	9	9	75	1	1	0	1	3	1	4
75	YSB	9	5	9	7	9	81	1	1	0	1	3	1	4
76	NR	12	5	9	9	10	85	1	1	0	2	4	2	6
77	GS	12	5	9	9	10	80	1	0	1	2	4	1	5
78	N	12	5	9	12	9	90	1	0	2	2	5	2	7
79	GS	12	5	3	12	9	75	1	1	1	1	4	3	7
80	AK	6	5	9	9	9	75	1	0	1	0	2	4	6
81	AB	12	5	6	9	9	81	0	2	1	2	5	4	9
82	PK	12	5	9	9	9	81	0	2	0	2	4	2	6
83	HS	12	5	5	9	9	75	1	1	1	1	4	3	7
84	VK	6	5	9	9	9	77	1	0	1	1	3	1	4
85	SG	12	5	5	9	9	75	2	1	0	1	4	2	6
86	MS	12	5	8	7	9	79	2	0	2	1	5	4	9
87	Y	12	5	8	9	9	81	3	1	1	1	6	3	9
88	NS	12	5	8	9	9	75	3	0	0	2	5	1	6
89	CS	12	5	8	13	9	89	2	1	1	2	6	3	9
90	MK	10	5	8	9	9	81	2	2	0	3	7	4	11
91	AS	11	5	8	9	9	86	2	0	2	1	5	4	9
92	MK	12	5	9	9	9	82	1	1	2	1	5	3	8
93	RS	9	5	5	12	9	74	2	0	1	2	5	4	9
94	LS	12	5	4	7	9	81	0	0	0	2	2	4	6
95	CK	12	5	7	12	9	86	0	0	1	1	2	4	6
96	PK	12	5	9	12	9	91	1	1	1	0	3	4	7
97	JS	10	5	8	12	9	91	0	1	1	0	2	4	6
98	JS	12	5	8	9	9	81	1	0	2	1	4	2	6
99	JR	10	5	3	13	9	87	2	0	0	1	3	1	4
100	AH	12	5	10	8	9	81	1	1	1	2	5	4	9
1	RK	10	5	9	8	9	91	-	-	-	-	-	-	-
2	AK	11	5	9	9	9	91	-	-	-	-	-	-	-
3	GS	11	5	9	8	9	91	-	-	-	-	-	-	-
4	NK	11	5	9	8	9	86	-	-	-	-	-	-	-
5	AS	11	5	9	9	10	82	-	-	-	-	-	-	-
6	GB	12	5	9	7	9	91	-	-	-	-	-	-	-

SR. NO	PATIENT NAME	MRD	GROUP	AGE	AGE GROUP	SEX	MARITAL STATUS	EDUCATION	OCCUPATION	EDUCATION GP	OCCUPATION GP	FAMILY TYPE	RELIGION	DURATION OF ILLNESS(IN YEARS)	FAMILY HISTORY OF PSYCHIATRIC ILLNESS	PREDOMINANT POLARITY	NO. OF MANIC EPISODES
7	RK		CONTROL	29	1	F	UNMARRIED	ILLITERATE	UNEMPLOYED	1	3	NUCLEAR	SIKH	-	-	-	-
8	LS		CONTROL	45	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	JOINT	SIKH	-	-	-	-
9	S		CONTROL	30	3	F	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	NUCLEAR	HINDU	-	-	-	-
10	HS		CONTROL	50	3	M	MARRIED	MATRICULATION	SKILLED WORKER	3	2	EXTENDED NUCLEAR	SIKH	-	-	-	-
11	BS		CONTROL	62	5	M	MARRIED	HIGHER SECONDARY	SEMI-PROFESSIONAL	2	5	EXTENDED NUCLEAR	SIKH	-	-	-	-
12	JK		CONTROL	28	1	F	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	NUCLEAR	SIKH	-	-	-	-
13	HS		CONTROL	60	4	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	SIKH	-	-	-	-
14	RK		CONTROL	52	4	F	MARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	SIKH	-	-	-	-
15	AK		CONTROL	35	2	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	SIKH	-	-	-	-
16	KS		CONTROL	31	2	M	UNMARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	NUCLEAR	SIKH	-	-	-	-
17	RK		CONTROL	28	1	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	JOINT	HINDU	-	-	-	-
18	KK		CONTROL	36	2	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	JOINT	SIKH	-	-	-	-
19	AG		CONTROL	31	2	F	MARRIED	POST-GRADUATE	PROFESSIONAL	5	4	NUCLEAR	HINDU	-	-	-	-
20	VPS		CONTROL	56	4	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	2	NUCLEAR	SIKH	-	-	-	-
21	MT		CONTROL	52	4	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	NUCLEAR	HINDU	-	-	-	-
22	CS		CONTROL	25	1	F	UNMARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	HINDU	-	-	-	-
23	AS		CONTROL	27	1	F	UNMARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	SIKH	-	-	-	-
24	KR		CONTROL	50	3	F	MARRIED	GRADUATE	PROFESSIONAL	4	4	NUCLEAR	HINDU	-	-	-	-
25	SK		CONTROL	50	3	F	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	NUCLEAR	SIKH	-	-	-	-
26	KF		CONTROL	61	5	F	MARRIED	GRADUATE	UNEMPLOYED	4	3	NUCLEAR	SIKH	-	-	-	-
27	D		CONTROL	45	3	M	MARRIED	HIGHER SECONDARY	BUSINESSMAN	2	1	NUCLEAR	HINDU	-	-	-	-
28	NS		CONTROL	60	4	M	MARRIED	ILLITERATE	SKILLED WORKER	1	2	NUCLEAR	SIKH	-	-	-	-
29	PS		CONTROL	50	3	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	SIKH	-	-	-	-
30	DK		CONTROL	58	4	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	NUCLEAR	SIKH	-	-	-	-
31	APS		CONTROL	18	1	M	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	2	8	NUCLEAR	SIKH	-	-	-	-
32	KK		CONTROL	26	1	F	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	NUCLEAR	SIKH	-	-	-	-
33	JK		CONTROL	33	2	F	MARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	EXTENDED NUCLEAR	SIKH	-	-	-	-
34	BK		CONTROL	30	1	F	MARRIED	MATRICULATION	UNEMPLOYED	3	3	NUCLEAR	SIKH	-	-	-	-
35	GS		CONTROL	45	3	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	NUCLEAR	SIKH	-	-	-	-
36	AK		CONTROL	62	5	M	MARRIED	HIGHER SECONDARY	SEMI-SKILLED	2	6	EXTENDED NUCLEAR	HINDU	-	-	-	-
37	VK		CONTROL	60	4	M	MARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	JOINT	HINDU	-	-	-	-
38	SS		CONTROL	58	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	EXTENDED NUCLEAR	SIKH	-	-	-	-
39	SS		CONTROL	52	4	M	MARRIED	GRADUATE	SKILLED WORKER	4	2	EXTENDED NUCLEAR	SIKH	-	-	-	-
40	JS		CONTROL	60	4	M	MARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	EXTENDED NUCLEAR	SIKH	-	-	-	-
41	SS		CONTROL	45	3	M	MARRIED	MATRICULATION	SKILLED WORKER	3	2	JOINT	SIKH	-	-	-	-
42	DJ		CONTROL	32	2	M	MARRIED	POST-GRADUATE	PROFESSIONAL	5	4	JOINT	HINDU	-	-	-	-
43	SG		CONTROL	35	2	F	MARRIED	POST-GRADUATE	UNEMPLOYED	5	3	EXTENDED NUCLEAR	HINDU	-	-	-	-
44	KK		CONTROL	52	4	F	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	2	3	NUCLEAR	SIKH	-	-	-	-
45	DA		CONTROL	38	2	M	MARRIED	GRADUATE	SEMI-PROFESSIONAL	4	5	NUCLEAR	HINDU	-	-	-	-
46	SK		CONTROL	35	2	F	MARRIED	GRADUATE	UNEMPLOYED	4	3	NUCLEAR	SIKH	-	-	-	-
47	BC		CONTROL	52	4	M	MARRIED	MATRICULATION	SKILLED WORKER	3	2	EXTENDED NUCLEAR	HINDU	-	-	-	-
48	AK		CONTROL	27	1	M	MARRIED	HIGHER SECONDARY	SKILLED WORKER	2	7	NUCLEAR	HINDU	-	-	-	-
49	MP		CONTROL	45	3	M	MARRIED	MATRICULATION	SKILLED WORKER	3	7	NUCLEAR	HINDU	-	-	-	-
50	SD		CONTROL	25	1	F	UNMARRIED	GRADUATE	SKILLED WORKER	4	7	NUCLEAR	SIKH	-	-	-	-

SR. NO	PATIENT NAME	NO. OF DEPRESSIVE EPISODES	Total episodes	NO. OF HOSPITALISATIONS	MOOD STABILISERS	TRAIL MAKING TEST SCORE- A	TRAIL MAKING TEST SCORE- B	DIGIT FORWARD	DIGIT BACKWARD	DIGIT SYMBOL SUBSTITUTION SCORE	STROOP COLOUR TEST SCORE- COLOUR SCORE	WORD SCORE	COLOUR-WORD SCORE	PREDICTED COLOUR WORD	INTERFERENCE SCORE	REMOTE MEMORY	RECENT MEMORY	MENTAL BALANCE	ATTENTION & CONCENTRATION	DELAYED RECALL
7	RK	-	0	-	-	35	89	6	3	72	75	64	40	34.5323741	5.467625899	5	5	7	18	10
8	LS	-	0	-	-	36	42	8	4	90	79	96	39	43.33714286	-4.337142857	4	5	9	19	10
9	S	-	0	-	-	38	56	5	5	76	74	56	40	31.87692308	8.123076923	7	4	9	15	10
10	HS	-	0	-	-	29	48	5	3	62	78	75	52	38.23529412	13.76470588	8	5	9	17	10
11	BS	-	0	-	-	40	112	4	6	65	85	85	53	42.5	10.5	8	5	9	17	10
12	JK	-	0	-	-	22	86	6	5	78	65	96	54	38.75776398	15.24223602	4	5	9	19	10
13	HS	-	0	-	-	23	74	5	4	76	88	68	51	38.35897436	12.64102564	8	5	9	15	10
14	RK	-	0	-	-	35	100	8	5	81	87	72	56	39.39622642	16.60377358	4	5	9	15	10
15	AK	-	0	-	-	39	90	7	3	63	75	73	42	36.99324324	5.006756757	4	5	9	18	10
16	KS	-	0	-	-	19	98	8	4	65	72	71	37	35.74825175	1.251748252	8	5	9	15	10
17	RK	-	0	-	-	18	65	7	5	70	70	69	38	34.74820144	3.251798561	4	5	9	20	10
18	KK	-	0	-	-	41	73	6	6	55	71	89	42	39.49375	2.50625	6	5	6	10	10
19	AG	-	0	-	-	22	74	6	7	53	65	90	53	37.74193548	15.25806452	6	4	8	9	10
20	VPS	-	0	-	-	24	72	7	4	54	64	100	55	39.02439024	15.97560976	6	4	9	9	10
21	MT	-	0	-	-	22	76	8	5	63	65	102	42	39.7005988	2.299401198	6	5	9	18	10
22	CS	-	0	-	-	23	84	5	3	68	63	68	39	32.70229008	6.297709924	6	5	9	19	10
23	AS	-	0	-	-	28	82	5	3	80	62	74	40	33.73529412	6.264705882	6	5	6	16	10
24	KR	-	0	-	-	36	46	5	4	91	61	71	56	32.81060606	23.18939394	5	5	6	10	10
25	SK	-	0	-	-	34	53	4	5	50	75	98	54	42.48554913	11.51445087	6	5	9	20	10
26	KF	-	0	-	-	29	86	5	5	58	74	96	36	41.78823529	-5.788235294	6	5	9	15	9
27	D	-	0	-	-	38	97	5	6	53	76	85	39	40.1242236	-1.124223602	5	5	8	9	10
28	NS	-	0	-	-	36	46	4	4	68	71	69	42	34.99285714	7.007142857	5	5	6	10	10
29	PS	-	0	-	-	40	62	5	5	75	65	59	46	30.92741935	15.07258065	4	5	6	14	10
30	DK	-	0	-	-	41	38	6	6	86	84	88	53	42.97674419	10.02325581	4	5	6	18	10
31	APS	-	0	-	-	40	66	6	4	72	80	57	51	33.28467153	17.71532847	6	5	9	10	10
32	KK	-	0	-	-	28	87	6	3	75	82	86	53	41.97619048	11.02380952	8	5	9	10	10
33	JK	-	0	-	-	20	84	7	4	46	80	74	38	38.44155844	-0.441558442	6	5	9	6	8
34	BK	-	0	-	-	22	96	5	5	66	86	75	39	40.0621118	-1.062111801	7	5	9	15	9
35	GS	-	0	-	-	27	99	8	6	68	84	76	40	39.9	0.1	6	5	5	19	10
36	AK	-	0	-	-	35	53	5	3	86	85	79	45	40.94512195	4.054878049	4	5	5	18	10
37	VK	-	0	-	-	29	65	5	4	66	67	72	43	34.70503597	8.294964029	6	5	9	15	10
38	SS	-	0	-	-	32	55	5	6	68	69	86	53	38.28387097	14.71612903	4	5	6	15	10
39	SS	-	0	-	-	37	76	6	5	74	62	81	38	35.11888112	2.881118881	6	5	9	15	10
40	JS	-	0	-	-	21	72	7	6	60	56	80	40	32.94117647	7.058823529	5	5	6	9	10
41	SS	-	0	-	-	27	74	8	5	72	58	68	52	31.3015873	20.6984127	4	5	8	14	10
42	DJ	-	0	-	-	32	70	8	4	76	60	63	55	30.73170732	24.26829268	6	5	5	15	10
43	SG	-	0	-	-	40	56	5	4	58	85	82	54	41.73652695	12.26347305	4	5	6	15	10
44	KK	-	0	-	-	18	84	6	5	63	84	84	43	42	1	6	5	5	17	10
45	DA	-	0	-	-	36	39	5	6	68	65	92	49	38.08917197	10.91082803	6	5	6	18	10
46	SK	-	0	-	-	43	109	4	4	69	68	94	57	39.45679012	17.54320988	5	5	5	15	10
47	BC	-	0	-	-	19	130	5	4	86	74	96	47	41.78823529	5.211764706	6	5	6	10	10
48	AK	-	0	-	-	27	79	6	5	79	79	77	56	38.99358974	17.00641026	6	5	5	17	10
49	MP	-	0	-	-	38	69	4	4	78	80	94	50	43.2183908	6.781609195	6	5	5	14	10
50	SD	-	0	-	-	26	44	5	5	70	84	88	40	42.97674419	-2.976744186	6	5	6	15	10

SR. NO	PATIENT NAME	IMMEDIATE RECALL	RETENTION FOR SIMILAR PAIRS	RETENTION FOR DISSIMILAR PAIRS	VISUAL RETENTION	RECOGNITION	LEVELS OF MEMORY	IDEAS- Self-care	Interpersonal activities	Communication and understanding	Work	Total score (A)	Duration of illness score (B)	Global score (A+B)
7	RK	12	5	9	7	10	88	-	-	-	-	-	-	-
8	LS	12	5	9	8	10	91	-	-	-	-	-	-	-
9	S	10	5	9	7	10	86	-	-	-	-	-	-	-
10	HS	12	5	9	7	9	91	-	-	-	-	-	-	-
11	BS	12	5	9	7	9	91	-	-	-	-	-	-	-
12	JK	12	5	9	8	10	91	-	-	-	-	-	-	-
13	HS	11	5	9	9	10	91	-	-	-	-	-	-	-
14	RK	12	5	9	8	9	86	-	-	-	-	-	-	-
15	AK	12	5	9	9	9	90	-	-	-	-	-	-	-
16	KS	12	5	9	8	10	91	-	-	-	-	-	-	-
17	RK	10	5	9	9	9	90	-	-	-	-	-	-	-
18	KK	11	5	15	8	8	84	-	-	-	-	-	-	-
19	AG	10	5	8	5	10	75	-	-	-	-	-	-	-
20	VPS	11	5	5	7	9	75	-	-	-	-	-	-	-
21	MT	12	5	9	7	9	90	-	-	-	-	-	-	-
22	CS	12	5	9	7	9	91	-	-	-	-	-	-	-
23	AS	12	5	9	8	8	85	-	-	-	-	-	-	-
24	KR	12	5	9	12	10	84	-	-	-	-	-	-	-
25	SK	11	5	6	8	10	90	-	-	-	-	-	-	-
26	KF	10	5	9	9	9	86	-	-	-	-	-	-	-
27	D	12	5	10	8	9	81	-	-	-	-	-	-	-
28	NS	12	5	9	11	10	83	-	-	-	-	-	-	-
29	PS	12	5	9	8	9	82	-	-	-	-	-	-	-
30	DK	12	5	8	8	9	85	-	-	-	-	-	-	-
31	APS	11	5	9	10	10	85	-	-	-	-	-	-	-
32	KK	12	5	8	10	9	86	-	-	-	-	-	-	-
33	JK	9	5	8	10	9	75	-	-	-	-	-	-	-
34	BK	9	5	8	10	9	86	-	-	-	-	-	-	-
35	GS	12	5	8	7	9	86	-	-	-	-	-	-	-
36	AK	12	5	9	7	9	84	-	-	-	-	-	-	-
37	VK	11	5	8	7	9	85	-	-	-	-	-	-	-
38	SS	11	5	7	9	9	81	-	-	-	-	-	-	-
39	SS	9	5	7	12	8	86	-	-	-	-	-	-	-
40	JS	10	5	8	8	9	75	-	-	-	-	-	-	-
41	SS	12	5	9	7	9	83	-	-	-	-	-	-	-
42	DJ	12	5	9	9	10	86	-	-	-	-	-	-	-
43	SG	12	5	9	8	10	84	-	-	-	-	-	-	-
44	KK	12	5	9	7	9	85	-	-	-	-	-	-	-
45	DA	11	5	9	7	9	86	-	-	-	-	-	-	-
46	SK	11	5	6	12	10	84	-	-	-	-	-	-	-
47	BC	11	5	9	8	9	79	-	-	-	-	-	-	-
48	AK	12	5	8	7	9	84	-	-	-	-	-	-	-
49	MP	11	5	9	7	9	81	-	-	-	-	-	-	-
50	SD	9	5	8	8	9	81	-	-	-	-	-	-	-

Email : [illegible]

No. BFUHS/2K21p-III/ 116 Date : 1/11/21

The Principal,
DMC, Ludhiana

Subject: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Aarti Gupta**, a student of your college for **MD Psychiatry** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

To study cognitive functions in patients of bipolar disorder in remission.

Supervisor
Dr. Ranjive Mahajan
Prof. & Head,
Dept. of Psychiatry,
DMCH, Ludhiana

Co-Supervisor

Dr. Navkiran Sooch Mahajan
Prof.,
Dept. of Psychiatry,
DMCH, Ludhiana.

The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

103. If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.

104. The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.

TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

Doctor of Medicine

in

PSYCHIATRY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

MARCH, 2021

DR. AARTI GUPTA

DEPARTMENT OF PSYCHIATRY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	'TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION'
For the degree of	MD PSYCHIATRY
Name of the candidate	DR. AARTI GUPTA
Supervisor	DR. RANJIVE MAHAJAN, PROFESSOR AND HEAD, DEPARTMENT OF PSYCHIATRY, DMCH
Co-supervisor	DR. NAVKIRAN SOOCH MAHAJAN, PROFESSOR DEPARTMENT OF PSYCHIATRY, DMCH
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction:The bipolar disorder is a chronic disorder with a high relapse rate, significant general disability, personal and social burden, and psychosocial impairment. Bipolar patients often suffer from "debilitating" cognitive impairment in different stages of the disease. Available evidence underscores that cognitive dysfunction is a critical mediator of adverse psychosocial outcomes in BD and a predictor of unfavorable employment outcomes. In this case-control study, we are studying cognitive functions in patients of Bipolar Disorder in remission and comparing it with healthy controls.

Aim of Study: To study cognitive functions in patients of Bipolar Disorder in remission.

Materials & methods: The study will be conducted on 100 patients in age group 18-65 years diagnosed as Bipolar Disorder in remission presenting to Department of Psychiatry, DMC&H Ludhiana and 50 healthy controls in the age group of 18-65 years. Age matched healthy controls will be recruited. Patients will be assessed in two clinical settings: **Clinical assessment**: Using Indian Disability Evaluation and Assessment Scale (IDEAS). The course of the illness will be assessed using National Institute of Mental Health- Life Chart Methology Clinician Retrospective Chart (NIHM-LCM) **Neuropsychological assessment:** Their cognitive functions will be assessed using neuropsychological assessment tests.

Clinical Significance: In this study, cognitive functions of patients of Bipolar Disorder in remission will be assessed and compared with healthy controls. The present study will suggest that Cognitive functioning may play an important role in the course and prognosis of bipolar patients and would contribute to better understanding of cognitive symptoms as a part of comprehensive treatment strategies.

Keywords: Cognitive functions, Bipolar Disorder, Course, Life Chart Method.

Signature (Candidate)	Signature (Supervisor)	Signature (Co-supervisor)	Signature (Principal)

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **'TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION'** exist in the Department of Psychiatry, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

Dr. Ranjive Mahajan
Professor & Head
Department of Psychiatry
DMCH, Ludhiana

Co-Supervisor(s)

Dr. Navkiran Sooch Mahajan
Professor
Department of Psychiatry
DMCH, Ludhiana

Head of the Department

Dr. Ranjive Mahajan
Professor & Head
Department of Psychiatry
DMCH, Ludhiana

Place : _____

Date : _____

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Aarti Gupta
Department	Psychiatry
Topic of Thesis	'TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION'
Likely date of appearing in PG examination	May – June 2023
Date of enrollment	26th July, 2020
Name of Head of Department	Dr. Ranjive Mahajan
1) Supervisor **2) Co-Supervisor**	Dr. Ranjive Mahajan Dr. Navkiran Sooch Mahajan
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. AARTI GUPTA 30-S, SANT NAGAR NEAR 21 NO. RAILWAY CROSSING, DIST- PATIALA 147001, PUNJAB.
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA (PUNJAB)
3	COURSE OF STUDY AND SUBJECT	M.D PSYCHIATRY
4	DATE OF ADMISSION OF COURSE	26.07.2020
5	TITLE OF THE TOPIC	“TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION”

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

The bipolar disorder is a chronic disorder with a high relapse rate, significant general disability, personal and social burden, and psychosocial impairment. The cognitive deterioration is often considered as a basic characteristic of this psychiatric disorder. Bipolar patients often suffer from “debilitating” cognitive impairment in different stages of the disease. Deficits in cognitive function are both transitory (acute phase of illness) and persistent (chronic/residual symptoms). Areas such as sustained attention, memory and executive function are involved. These deficits are present during the acute phase of illness and persist through-out periods of euthymia. The mood changes in acute episodes have a clear impact on cognitive functioning.[1] Current symptoms, past course of illness, clinical features such as the presence of psychosis and co-morbid conditions may all influence cognitive function in mood disorders With regard to psychiatric disorders, cognitive functions has been scarcely studied, but it is present implicitly in a large number of studies assessing premorbid intelligence as a key role in the development and outcome of psychiatric disorders.[2] Cognitive functioning may contribute to functional outcome in Bipolar Disorder and may be applied in research and clinical interventions to prevent cognitive and functional impairment. Despite the general lack of assessment of cognitive function in clinical practice, clinicians are increasingly targeting cognitive symptoms as part of comprehensive treatment strategies.[3] It is worth mentioning that neurocognitive impairment needs to be considered a therapeutic clinical target in order to improve both psychosocial functioning and quality of life of patients with BD (Grande et al., 2016).[4] Available evidence underscores that cognitive dysfunction is a critical mediator of adverse psychosocial outcomes in BD and a predictor of unfavorable employment outcomes (Tse et al., 2014; Baune and Malhi, 2015;).[5] Similar to cognitive dysfunction, functional deficits persist even after symptomatic remission in a significant subset of patients with BD, thus aggregating additional burden to patients and also possi-

bly increasing illness-related direct and indirect costs. In this sense, BD is ranked among the leading causes of burden of disease worldwide associated with a high level of disability-adjusted life years.[6] Despite the growing awareness of the critical importance of neurocognitive functioning to BDs' outcome, data on the longitudinal trajectory of cognitive deficits across the course of the illness are scarce and inconsistent.[7] There is a paucity of research about the course of bipolar disorder in tropical countries including India. Though studies in the west have progressed from chart based studies to long term cohorts including assessment of weekly mood state by 6 monthly retrospective recalls (Judd et al., 2003, 2002)[8], there is a lack of longer term studies of the course and outcome of adults with bipolar disorder from India, and sample sizes in these studies have generally been small (Chopra et al., 2006)[9]. In the absence of prospective data, systematic retrospective studies can be a useful foundation for robust and large-scale prospective studies to emerge. Given the lack of systematic data on the course of bipolar disorder in this setting, we planned to characterize the course of this disorder among patients attending a tertiary care center using a widely accepted retrospective life chart method in this case-control study.[10] Broadening our knowledge on the longitudinal course of cognition in BD is an indispensable step towards having a complete description of these disorders. It would contribute to better understanding of the pathophysiological mechanisms sub-serving BDs, to identify targets for treatment, to determine possible subtypes of the disorder, and to develop better therapeutic strategies.[7] This proposal seeks to build on prior research to assess cognitive functioning in Bipolar disorder. It would contribute to better understanding of cognitive symptoms as a part of comprehensive treatment strategies.

6.2 REVIEW OF LITERATURE

Bipolar disorder is a mood disorder involving a range of manic symptoms typically preceded by and interspersed with depressive episodes. Although a lifetime prevalence of 1% is often quoted for bipolar disorder with manic states (DSM-IV bipolar I), when subsyndromal manic symptoms (DSM-IV bipolar II, bipolar disorder not otherwise specified [NOS], and cyclothymic disorder) are included, its prevalence is seen to be higher than 6%.[11]

Regarding cognitive functions, the studies done by Anaya et al. showed clear positive association between CR and each of the assessed domains. Hence, a bipolar patient with a higher CR maintains better capacities of attention, processing speed and working memory, concentration, verbal and visuospatial memory and executive functions, independently of the possible effects of age and chronicity. These results would be in line with the hypothesis that a higher CR implies a more efficient utilization of brain networks. Our results also indicate a positive relationship between CR and psychosocial functioning, patients with a higher CR showing a better psychosocial functioning. Cognitive functions have been found to modulate psychosocial functioning, with the latest research highlighting that verbal memory seems to be the main cognitive capacity influencing the functioning of patients with BD.[12]

In studies conducted by Dittmann et al; The multivariate analysis of covariance (MANCOVA) indicated overall differences in neuropsychological performance between the three groups. Patients with bipolar I disorder showed significantly lower scores in psychomotor speed, working memory, verbal learning, delayed memory, and executive functions than healthy controls. Patients with bipolar II disorder showed significant deficits in psychomotor speed, working memory, visual／constructional abilities, and executive functions compared to controls, but not on verbal learning and delayed memory. The two patient groups did not differ significantly from each other on any domain tested.[13]

In studies conducted by Chopra et al; Seven (26%) of the 27 patients evaluated directly had not received any treatment whatsoever. Four patients (15%) had experienced rapid-cycling at some time; patients without rapid-cycling had experienced a mean 0.22 episodes/year. Episodes of mania accounted for 72% of all episodes. None of the variables examined appeared to predict the total number of episodes experienced by individual patients, although rapid-cycling occurred significantly more often if the patients had not received any psychopharmacological treatment.[9]

Carlson et al. (60) followed 53 bipolar patients for a mean of 3.2 years and also found that approximately one-third of patients had impaired occupational and social functioning.[14]

The meta-analysis of neuropsychological performance in euthymic bipolar disorder conducted by Mann-Wrobel et al. revealed considerable impairments in these individuals compared to control subjects. Their findings, however, do not support a conclusion that domains of verbal memory and executive functioning are differentially impaired in this population, as some have proposed .Rather, generally comparable impairment was observed across domains in current data, with the exception of more crystallized verbal abilities. Similarly though less severely than in schizophrenia, it appears there is a broadly generalized cognitive impairment in euthymic bipolar disorder, with verbal ability as a possible area of preserved performance.[15]

A naturalistic course of bipolar disorder in rural India was reported by Chopra M P *et al*. This data is from the Primary Health Centre, Sakalwara, adapted at NIMHANS, 27 patients of 34 patients evaluated had not received any treatment at all, though there were many episodes. 15% of patient has had rapid cycling, episodes of manic accounted for 72% of episodes. None of the variables examined could predict the total number of episodes. However, patients receiving psycho pharmacological agents are likely to develop rapid cycling. A mania predominant course was observed in this study cohort.[16]

Predominant polarity during the course of bipolar disorder seems to have important clinical and therapeutic implications. Polarity of the first

mood episode determined the predominant polarity during the course. Turvey et al. reported that the polarity sequences tend to remain stable overtime(Turveyetal.,1999).In a study by Perlis et al., 62% of patients whose initial episode was mania had a predominantly mania course(Perlisetal.,2005).Other studies have also demonstrated that initial episode polarity determines the predominant polarity during the course, i.e.initial episode of mania and depression determine the predominantly manic and depressive course, respectively (Baldessarinietal.,2012; Colometal.,2006; Popovicetal.,2014).[17]

There are three main findings in the study conducted by Pålsson et al. First, the study confirmed previous findings that clinically stable patients with bipolar disorder showed impairment in inhibition, in set-shifting, in verbal fluency and in visual recall compared to healthy age-matched controls. Bipolar patients also gave more rapid responses during the Tower test and showed impulsivity on the Color-word test, yet were slower in drawing the Rey figure. Second, there were no major differences between the type I and type II subtypes of bipolar disorder. Third, treatment with antipsychotic drugs was associated with worse performance in verbal fluency, in inhibition, in set-shifting and a longer time to draw the Rey figure.[18]

6.3 AIMS AND OBJECTIVES OF THE STUDY

To study cognitive functions in patients of Bipolar Disorder in remission.

7. MATERIALS AND METHODS

7.1 Source of Data

Study will be conducted on patients diagnosed as Bipolar Disorder presenting to DMC&H, Ludhiana.

7.2 METHOD OF COLLECTION OF DATA

SAMPLE COLLECTION- The study would include 100 patients in age group of 18-65 years with Bipolar Disorder currently in remission presenting to the Department Of Psychiatry in DMC&H Hospital, Ludhiana and 50 controls in age group 18-65 years of age.

INCLUSION CRITERIA:

FOR CASES:

1. The patients with a diagnosis of Bipolar Disorder according to DSM-5 criteria presenting to DMC&H, Ludhiana.
2. Age group between 18 years to 65 years.
3. Duration of illnesss of atleast one year.
4. Patients who have given consent for the study.

FOR CONTROLS:

1. The patients not having any history of bipolar disorder or any other psychiatric illness.
2. Age group between 18 years to 65 years.
3. Individuals who have given consent for the study.

EXCLUSION CRITERIA

FOR CASES:

1. Any other major psychiatric disorder in patients of Bipolar Disorder on AXIS I.
2. Suffering from an organic brain syndrome.
3. Patients who have not given consent for the study.
4. Duration of illness less than one year.

FOR CONTROLS:

1. Any on-going psychiatric or neurological disorder
2. Current treatment with any psychotropic drugs.
3. Past history of bipolar disorder, schizophrenia, recurrent depression or other psychiatric disorder.

4. A first-degree relative with schizophrenia or bipolar disorder

METHODOLOGY

The study will be conducted on 100 patients in age group 18-65 years diagnosed as Bipolar Disorder in remission presenting to Department of Psychiatry, DMC&H Ludhiana and 50 healthy controls in age group 18-65 years. Age matched healthy controls will be recruited. To be eligible, patients have to meet the inclusion criteria and provide written informed consent before enrolment. Their cognitive functions will be assessed using neuropsychological assessment tests. The Functional assessment will be assessed using Indian Disability Evaluation and Assessment Scale (IDEAS). The course of the illness will be assessed using National Institute of Mental Health- Life Chart Methodology Clinician Retrospective Chart (NIHM-LCM).

TOOLS:

SOCIODEMOGRAPHIC PERFORMA

1) CLINICAL ASSESSMENT

Indian Disability Evaluation and Assessment Scale (IDEAS):

It evaluates disability in four areas (termed items in the scale), namely, self care, interpersonal activities, communication and understanding, and work. Each item is scored on a 5 point scale with a range of 0-4, i.e. from no (0) to profound disability (4).

National Institute of Mental Health- Life Chart Methology Clinician Retrospective Chart (NIHM-LCM):

The clinician rated scale charts the phases of the illness for the entirety of a patient's life. Charting may start with the first / index episode mentioning its polarity, and progresses alone each episode , this method allows specification of the type of episode, its duration and severity. It also allows the coding of comorbid symptoms , triggering life events , hospitalization , medication use and other elevent details.

2) NEUROPSYCHOLOGICAL ASSESSMENT

a) Attention:

TRIAL MAKING TEST:

The trail making test (TMT) is a brief paper and pencil neuropsychological test often used for screening for cognitive impairment. The TMT

was a standard component of the Halstead-Reitan Battery which measures cognitive dysfunction.

DIGIT SPAN:

The Digit Span test is a subtest of both the Wechsler Adult Intelligence Scale (WAIS) and the Wechsler Memory Scales (WMS).Forward span captures attention efficiency and capacity. Backward span is an executive task particularly dependent on working memory.

b) Processing Speed: DIGIT SYMBOL CODING

The DSST is a paper-and-pencil cognitive test presented on a single sheet of paper that requires a subject to match symbols to numbers according to a key located on the top of the page. The subject copies the symbol into spaces below a row of numbers. The number of correct symbols within the allowed time, usually 90 to 120 seconds, constitutes the score.

c) Memory: POSTGRADUATE INSTITUTE (PGI) MEMORY SCALE :

The Postgraduate Institute (PGI) memory scale is part of the PGI battery of brain dysfunction, and has been developed in India. It is a comprehensive scale to measure verbal and non-verbal memory and has been extensively used in Indian studies. It consists of 10 sub-tests: remote memory, recent memory, mental balance, attention and concentration (Digit span), immediate recall, verbal retention for similar pairs, verbal retention for dis-similar pairs, visual retention and recognition.

d) Executive function: Stroop Colour Word Test (SCWT):

The Stroop Color and Word Test (SCWT) measures the relative speeds of reading the names of colors (word card), naming colors (color card), and identifying color names that are printed in another color(interference card).The test is essentially a measure of cognitive flexibility and response inhibition.

OUTCOME

In this case-control study, cognitive functions in patients with bipolar disorder will be assessed and compared with healthy controls. The

present study will suggest that Cognitive functioning may play an important role in the course and prognosis of bipolar patients and it should be considered in both clinical and research setting related to bipolar disorder.

Statistical Analysis

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5. A probability value (p value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

NO.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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SOCIO DEMOGRAPHIC PROFILE

S.No.

DATE-

NAME AGE GENDER

MRD NO.

MARITAL STATUS

Education- a) Illiterate b) Upto Matriculation

c) Higher secondary d) Graduate/Post-Graduate

Occupation-

a) Unemployed b) Semi-skilled/skilled worker

c) Business/ Job d) Other.

INCOME:

TYPE OF FAMILY- JOINT/NUCLEAR/LIVING ALONE

ADDRESS

CONTACT NO.

DIAGNOSIS BY DSM-V:

DURATION OF ILLNESS /COURSE OF ILLNESS:

FAMILY HISTORY OF BIPOLAR DISORDER:

TRAIL MAKING TEST SCORE:

DIGIT SPAN SCORE:

DIGIT SYMBOL SUBSTITUTION TEST SCORE:

PGI MEMORY SCALE

STROOP COLOUR TEST SCORE:

IDEAS SCORE:

SIGNATURE OF CANDIDATE **SIGNATURE OF SUPERVISOR**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....am willing to participate in the study **"TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

फार्म अनुमति मरीज

तिथि_____

मैं_____ पत्नी/पुत्र/ पुत्री_____

निवासी_____

इस शोधकार्य **"TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION"** सहमत लिए के लेने भाग में मैं हूँ। तैयार से स्वेच्छा अपनी लिए के लेने भाग में शोधकार्य इस मैं हूँ। करता पुष्टि/ प्रलोभन आर्थिक कोई मुझे लिए के देने स्वीकृति यह की हूँ करती श्यउद्दे का शोधकार्य इस मुझे है। गया डाला दबाव ही न और गया दिया नहीं और विज्ञान यह की है सविश्वा यह मुझे और है गया दिया कर स्पष्ट बारे के जोखिम वाले होने में शोधकार्य इस मुझे है। लिए के लाभ के मानवता है। मामुली बहुत जोखिम यह में समझ मेरी और है गया दिया समझा में

अपनी समय भी किसी में सम्बन्ध के लेने भाग में शोधकार्य इस मैं सकता कर व्यक्त अस्वीकृति/ का करने व्यक्त अस्वीकृति मेरे और हूँ सकती पड़ेगा। नहीं प्रभाव कोई पर इलाज मेरे

_____ _____

हस्ताक्षर के गवाह हस्ताक्षर के रोगी/ निशान का अंगूठे

नाम: नाम:

_____

अन्वेषक केहस्ताक्षर

_____

हस्ताक्षर के विद्यार्थी

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ_____

"TO STUDY COGNITIVE FUNCTIONS IN PATIENTS OF BIPOLAR DISORDER IN REMISSION" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ ।ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ ।ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ ।ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

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ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ

_____
ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

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ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

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ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ